Intramolecular Hydrogen Bond Activation for Kinetic Resolution of Furanone Derivatives by an Organocatalyzed [3+2] Asymmetric Cycloaddition

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Table of Contents

Experimental Procedures.

The ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a *Bruker Avance 300 MHz spectrometer* running at 300 MHz for ^{1}H and 75 MHz for ^{13}C or on a *Bruker DRX-500 spectrometer* running at 126 MHz for ^{13}C and 471 MHz for ^{19}F coupled mode, respectively. The chemical shifts (δ) are reported relative to the tetramethylsilane signal at 0 ppm or relative to the residual signal of the solvent ($CDCl_3$ at 7.26 ppm), ($(CD_3)_2SO$) at 2.50 ppm), (CD_2Cl_2 at 5.32 ppm), (CD_3CN at 1.94 ppm) while for ^{13}C-NMR are given in ppm relative to the residual signal of solvent ($CDCl_3$ at 77.16 ppm), ($(CD_3)_2SO$) at 39.5 ppm), (CD_2Cl_2 at 53.84 ppm), (CD_3CN at 1.32 ppm and 118.26 ppm) ^{13}C NMR spectra were acquired on a broadband decoupled mode. ^{19}F NMR were acquired on a broadband decoupled and coupled mode indicated in each case. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; dd, doublet of doublets; ddd, doublet of doublet of doublets; t, triplet; dt, doublet of triplets; td, triplet of doublets; tt, triplet of triplets; q, quartet; dq, doublet of quartets; p, pentet; sept, septet; m, multiplet; br, broad signal. The following abbreviations are used to indicate the solvents: Cy, Cyclohexane; DCM, dichloromethane, EtOH, Ethanol; EtOAc, Ethyl acetate; MeOH, Methanol; THF, Tetrahydrofuran.

Optical rotations were measured on an Anton Paar NCP 100 Polarimeter at room temperature and and $[\alpha]^{20}_{D}$ values are given in deg·mL·g^{-1}·dm^{-1}; concentration *c* is listed in g·(100 mL)$^{-1}$.

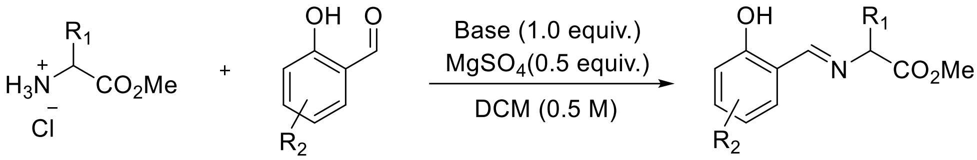
Enantiomeric excess was determined on an *SFC Agilent Technologies 1260 Infinity Series* instrument equipped with a UV-VIS detector, employing *Daicel Chiralpak* IA, IB-3, IC, ID, and IG-3 columns as chiral stationary phase. The exact conditions for the analyses are specified in each case.

High-Resolution Mass Spectra (HRMS) were obtained on an *Agilent Technologies 6120 Quadrupole LC/MS* coupled with an *SFC Agilent technologies 1260 Infinity Series* instrument for the ESI-MS (Electrospray Ionization). *MassWorks* software version 4.0.0.0 (*Cerno Bioscience*) was used for the formula identification. *MassWorks* is an MS calibration software which calibrates isotope profiles to achieve high mass accuracy and enables elemental composition determination on conventional mass spectrometers of unit mass resolution allowing highly accurate comparisons between calibrated and theoretical spectra.[1]

Commercial grade reagents and solvent were purchased from *Sigma-Aldrich*, *Alfa Aesar*, *Fluorochem*, *TCI Chemicals* and used without further purifications while anhydrous solvents were taken from a SPS solvent dispenser. Racemic samples were prepared from a 1:1 mixture of compounds using (*S,S*) and (*R,R*) catalysts. Analytical TLC was performed using pre-coated aluminium-backed plates (*Merck TLC Silicagel* 60 F_{254}) and visualized by ultraviolet irradiation. Chromatographic purification of products was accomplished using flash column chromatography (FC) on Merck Geduran® Si 60 silica gel (40 – 63 μm), or Iatrobeads 6RS –8060 (*Iatroscan*), or Florisil® 100-200 mesh (*Thermoscientific*). Celite® *512 medium* (*Sigma-Aldrich*) was used for filtration. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator.

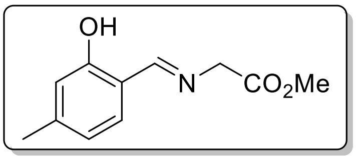
Commercially available reagents and catalyst were used without further purification. Racemic samples were prepared using a 1:1 mixture of both catalyst enantiomers. Aldimines **1a**,[2] **1b**, **1j**, **1k**, **1m**, **1n** and **1o**[3] **1f**,[4] **1p**[5] and **1r**[6] have been synthesized following the general procedure (GP1), described before, and their spectroscopic data are in agreement with published data. 5-Methoxy-2(5*H*)-furanone (**(±)-2a**),[7] 5-ethoxy-2(5*H*)-furanone (**(±)-2b**),[8] 5-(ethylthio)furan-2(5*H*)-one (**(±)-2c**)[9] and 3-bromo-5-methoxy-2(5*H*)-furanone (**(±)-2d**)[10] were synthesized following the procedures described in the literature.

General Procedure (GP1) for the Synthesis of Imines 1.



Base (1.0 equiv.) and $MgSO_4$ were added to a solution of the corresponding glycine ester hydrochloride (1.0 equiv.) in DCM ([0.5]M). The mixture was stirred at rt for 1 h. Then, the corresponding aldehyde (1.02 equiv.) was added, and the mixture was stirred at rt for 24-48h followed by TLC. The suspension was filtered and concentrated in vacuum. The residue was dissolved in water and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. The product was used without further purification or purified by flash column chromatography specified in each case on Florisil.

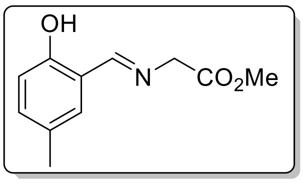
Methyl (*E*)-2-((2-hydroxy-4-methylbenzylidene)amino)acetate (**1c**):



The reaction of 2-hydroxy-4-methylbenzaldehyde (416.1 mg, 3.06 mmol), methyl glycinate hydrochloride (376.6 mg, 3 mmol), $MgSO_4$ (180.5 mg, 1.5 mmol) and Et_3N (0.42 mL, 3 mmol) in CH_2Cl_2, following the general procedure **GP1** and purification by flash column chromatography (Cy:EtOAc = 80:20), yielded de compound **1c** as a yellow solid (279.8 mg, 45% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ: 12.87 (brs, 1H), 8.25 (s, 1H), 7.10 (d, J = 7.8 Hz, 1H), 6.76 (s, 1H), 6.67 (d, J = 7.8 Hz, 1H), 4.31 (s, 2H), 3.73 (s, 3H), 2.30 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 169.8, 168.2, 160.9, 143.7, 131.5, 119.8, 117.3, 116.2, 59.5, 52.1, 21.7. **ESI-HRMS** calculated for $C_{11}H_{14}NO_3$ $(M+H)^+$: 208.0968; found: 208.0962.

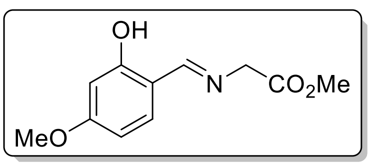
Methyl (*E*)-2-((2-hydroxy-5-methylbenzylidene)amino)acetate (**1d**):



The reaction of 2-hydroxy-5-methylbenzaldehyde (416.1 mg, 3.06 mmol), methyl glycinate hydrochloride (376.6 mg, 3 mmol), $MgSO_4$ (180.5 mg, 1.5 mmol) and Et_3N (0.42 mL, 3 mmol) in CH_2Cl_2, following the general procedure **GP1** and purification by flash column chromatography (Cy:EtOAc = 80:20), yielded de compound **1d** as a yellow solid (348.1 mg, 56% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ: 12.72 (s, 1H), 8.33 (s, 1H), 7.17 (dd, J = 8.4, 2.2 Hz, 1H), 7.08 (d, J = 2.2 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 4.40 (s, 2H), 3.81 (s, 3H), 2.32 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 169.8, 168.6, 158.8, 133.7, 131.8, 127.8, 118.3, 116.9, 59.8, 52.2, 20.3. **ESI-HRMS** calculated for $C_{11}H_{14}NO_3$ $(M+H)^+$: 208.0968; found: 208.0978.

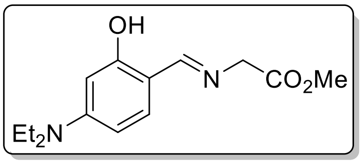
Methyl (*E*)-2-((2-hydroxy-4-methoxybenzylidene)amino)acetate (**1e**):



The reaction of 2-hydroxy-4-methoxybenzaldehyde (465.6 mg, 3.06 mmol), methyl glycinate hydrochloride (376.6 mg, 3 mmol), $MgSO_4$ (180.5 mg, 1.5 mmol) and Et_3N (0.42 mL, 3 mmol) in CH_2Cl_2, following the general procedure **GP1** and purification by flash column chromatography (Cy:EtOAc = 70:30), yielded de compound **1e** as a yellow solid (414.9 mg, 62% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ: 13.37 (brs, 1H), 8.25 (s, 1H), 7.15 (d, J = 8.4 Hz, 1H), 6.48 (d, J = 2.4 Hz, 1H), 6.44 (dd, J = 8.4, 2.4 Hz, 1H), 4.34 (s, 2H), 3.82 (s, 3H), 3.78 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 170.0, 167.6, 163.9, 163.7, 133.0, 112.5, 106.7, 101.1, 59.3, 55.4, 52.3. **ESI-HRMS** calculated for $C_{11}H_{14}NO_4$ $(M+H)^+$: 224.0917; found: 224.0903.

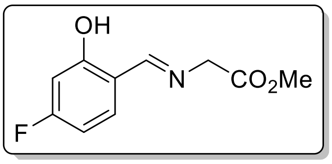
Methyl (*E*)-2-((4-(diethylamino)-2-hydroxybenzylidene)amino)acetate (**1g**):



The reaction of 4-(diethylamino)-2-hydroxybenzaldehyde (591.3 mg, 3.06 mmol), methyl glycinate hydrochloride (376.6 mg, 3 mmol), $MgSO_4$ (180.5 mg, 1.5 mmol) and Et_3N (0.42 mL, 3 mmol) in CH_2Cl_2, following the general procedure **GP1** and purification by flash column chromatography (Cy:EtOAc = 70:30), yielded de compound **1g** as a yellow solid (301.3 mg, 38% yield).

^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 13.29 (brs, 1H), 8.14 (s, 1H), 7.06 (d, *J* = 8.6 Hz, 1H), 6.25 – 6.10 (m, 2H), 4.31 (s, 2H), 3.79 (s, 3H), 3.40 (q, *J* = 7.1 Hz, 4H), 1.21 (t, *J* = 7.1 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 170.5, 166.9, 164.0, 151.5, 133.1, 108.4, 103.2, 97.9, 59.1, 52.1, 44.5, 12.7. **ESI-HRMS** calculated for $C_{14}H_{21}N_2O_3$ $(M+H)^+$: 265.1547; found: 265.1557.

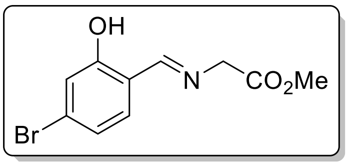
Methyl (*E*)-2-((4-fluoro-2-hydroxybenzylidene)amino)acetate (**1h**):



The reaction of 4-fluoro-2-hydroxybenzaldehyde (428.7 mg, 3.06 mmol), methyl glycinate hydrochloride (376.6 mg, 3 mmol), $MgSO_4$ (180.5 mg, 1.5 mmol) and Et_3N (0.42 mL, 3 mmol) in CH_2Cl_2, following the general procedure **GP1** and purification by flash column chromatography (Cy:EtOAc = 80:20), yielded de compound **1h** as a yellow solid (291.4 mg, 46% yield).

^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 8.30 (s, 1H), 7.26–7.19 (m, 1H), 6.66 – 6.53 (m, 2H), 4.35 (s, 2H), 3.77 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 169.7, 167.7, 165.7 (d, *J* = 252.1 Hz), 163.8 (d, *J* = 13.9 Hz), 133.6 (d, *J* = 11.7 Hz), 115.5, 106.6 (d, *J* = 23.2 Hz), 104.4 (d, *J* = 23.6 Hz), 59.2, 52.5. **ESI-HRMS** calculated for $C_{10}H_{11}FNO_3$ $(M+H)^+$: 212.0717; found: 212.0729.

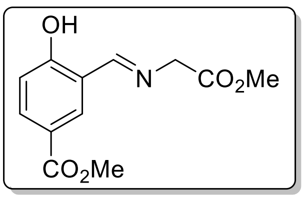
(*E*)-Methyl-2-((4-bromo-2-hydroxybenzylidene)amino)acetate (**1i**):



The reaction of 4-bromo-2-hydroxybenzaldehyde (615.1 mg, 3.06 mmol), methyl glycinate hydrochloride (376.6 mg, 3 mmol), $MgSO_4$ (180.5 mg, 1.5 mmol) and Et_3N (0.42 mL, 3 mmol) in CH_2Cl_2, following the general procedure **GP1** and purification by flash column chromatography (Cy:EtOAc = 80:20), yielded de compound **1i** as a yellow solid (481.6 mg, 59% yield).

^{1}H NMR (300 MHz, $CDCl_3$) *δ*: δ 8.25 (s, 1H), 7.10 (d, *J* = 1.9 Hz, 1H), 7.05 (d, *J* = 8.2 Hz, 1H), 6.95 (dd, *J* = 8.2, 1.9 Hz, 1H), 4.35 (s, 2H), 3.75 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 169.5, 167.8, 162.2, 132.8, 127.3, 122.0, 120.6, 117.3, 59.1, 52.4. **ESI-HRMS** calculated for $C_{10}H_{11}BrNO_3$ $(M+H)^+$: 271.9917 and 273.9897; found: 271.9931: 273.9911.

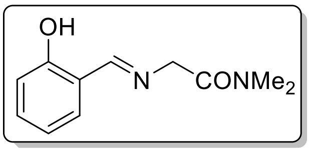
Methyl (*E*)-4-hydroxy-3-(((2-methoxy-2-oxoethyl)imino)methyl)benzoate (**1l**):



The reaction of methyl 3-formyl-4-hydroxybenzoate (551.3 mg, 3.06 mmol), methyl glycinate hydrochloride (376.6 mg, 3 mmol), $MgSO_4$ (180.5 mg, 1.5 mmol) and Na_2CO_3 (317.9 mg, 3 mmol) in CH_2Cl_2, following the general procedure **GP1** and purification by flash column chromatography (Cy:EtOAc = 80:20), yielded de compound **1l** as a yellow solid (376.8 mg, 50% yield).

^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 13.57 (brs, 1H), 8.36 (s, 1H), 8.00 – 7.91 (m, 2H), 6.94 (d, *J* = 9.1 Hz, 1H), 4.38 (s, 2H), 3.84 (s, 3H), 3.74 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 169.4, 168.1, 166.2, 165.2, 134.1, 120.8, 118.0, 117.4, 59.3, 52.4, 52.0. **ESI-HRMS** calculated for $C_{12}H_{14}NO_5$ $(M+H)^+$: 252.0866; found: 252.0876.

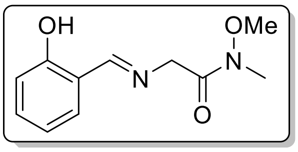
(*E*)-2-((2-hydroxybenzylidene)amino)-*N,N*-dimethylacetamide (**1q**):



The reaction of 2-hydroxybenzaldehyde (373.7 mg, 3.06 mmol), 2-amino-*N,N*-dimethylacetamide hydrochloride (415.8 mg, 3 mmol), $MgSO_4$ (180.5 mg, 1.5 mmol) and Et_3N (0.42 mL, 3 mmol) in CH_2Cl_2, following the general procedure **GP1** and purification by flash column chromatography (Cy:EtOAc = 80:20), yielded de compound **1q** as a yellow solid (259.9 mg, 42% yield).

^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 12.94 (s, 1H), 8.32 (s, 1H), 7.28 – 7.19 (m, 2H), 6.89 (d, *J* = 8.3 Hz, 1H), 6.81 (t, *J* = 7.4 Hz, 1H), 4.35 (s, 2H), 3.04 (s, 3H), 2.90 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 168.1, 168.0, 160.8, 132.5, 131.6, 118.6, 118.6, 116.8, 60.5, 36.9, 35.4. **ESI-HRMS** calculated for $C_{11}H_{15}N_2O_2$ $(M+H)^+$: 207,1128; found: 207.1114.

(*E*)-2-((2-hydroxybenzylidene)amino)-*N*-methoxy-*N*-methylacetamide (**1s**):



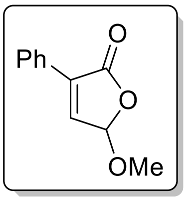
Tert-butyl (2-(methoxy(methyl)amino)-2-oxoethyl)carbamate (655mg, 3 mmol) was dissolved in 2.5 mL of $CHCl_3$ and stirred for 5 min at 0 °C. Then, HCl 1M in Et_2O (25mL) was added dropwise. The reaction was followed by TLC. The white solid formed was filtered and used without further purification in the next step. The reaction of 2-hydroxybenzaldehyde (373.7 mg, 3.06 mmol), 2-(methoxy(methyl)amino)-2-oxoethanaminium hydrochloride (463.8 mg, 3 mmol), $MgSO_4$ (180.5 mg, 1.5 mmol) and Et_3N (0.42 mL, 3 mmol) in CH_2Cl_2, following the general procedure **GP1** and purification by flash column chromatography (Cy:EtOAc = 90:10), yielded de compound **1s** as a yellow solid (433.4 mg, 60% yield).

^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 8.41 (s, 1H), 7.36 – 7.28 (m, 2H), 6.98 (d, *J* = 8.2 Hz, 1H), 6.88 (td, *J* = 7.5, 1.1 Hz, 1H), 4.53 (s, 2H), 3.77 (s, 3H), 3.25 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ* (ppm):169.7, 168.9, 161.3, 132.8, 131.8, 118.9, 118.8, 117.3, 61.8, 58.99, 29.9. **ESI-HRMS** calculated for $C_{11}H_{15}N_2O_3$ $(M+H)^+$: 223,1077; found: 223.1073.

General Procedure (GP2) for the Synthesis of Dipolarophiles (±)-2e-g

Cesium fluoride (0.563 g, 3.71 mmol), $BnNEt_3Cl$ (0.014 g, 0.061 mmol), corresponding boronic acid (2.47 mmol), and $PdCl_2(PPh_3)_2$ (0.043 g, 0.061 mmol) were dissolved in 10 mL of degassed water. The mixture was further degassed by evacuation and back-fill with N_2 five times. Degassed toluene (5 mL) was added to the reaction mixture followed by dropwise addition of 3-bromo-5-methoxyfuran-2(5*H*)-one (**(±)-2d**) (0.250 g, 1.30 mmol) in degassed toluene (5 mL). The reaction mixture was heated to reflux for 12 h. The reaction was cooled to room temperature, washed with water, and extracted three times with ethyl acetate. The combined organic phases were dried over $MgSO_4$ and concentrated in vacuum. Purification by flash column chromatography on Iatrobeads silica gel with the indicated eluent.

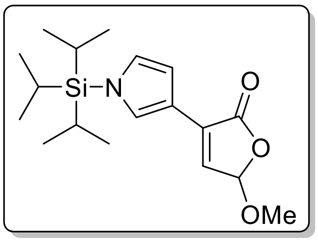
5-Methoxy-3-phenylfuran-2(5*H*)-one (**(±)-2e**):



The reaction was carried out using phenylboronic acid (0.301 g, 2.47 mmol) following the general procedure **GP2**. Purification by flash column chromatography on Iatrobeads silica gel (Cy:EtOAc = 95:5) yielded the compound **(±)-2e** as a yellow oil (148.2 mg, 60% yield).

^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 7.90 – 7.80 (m, 2H), 7.45 – 7.40 (m, 3H), 7.27 (d, *J* = 1.4 Hz, 1H), 5.88 (d, *J* = 1.4 Hz, 1H), 3.63 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 169.6, 141.2, 135.5, 130.2, 128.9, 127.7, 101.7, 57.1. **ESI-HRMS** calculated for $C_{11}H_{11}O_3$ $(M+H)^+$: 191.0703; found: 191.0709.

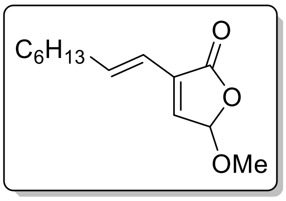
5-Methoxy-3-(1-(triisopropylsilyl)-1*H*-pyrrol-3-yl)furan-2(5*H*)-one (**(±)-2f**):



The reaction was carried out using (1-(triisopropylsilyl)-1*H*-pyrrol-3-yl)boronic acid (0.660 g, 2.47 mmol) following the general procedure **GP2**. Purification by flash column chromatography on Iatrobeads silica gel (Cy:EtOAc = 95:5) yielded the compound **(±)-2f** as a brown oil (174.3 mg, 40% yield).

^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 7.61 (s, 1H), 6.85 (d, *J* = 1.7 Hz, 1H), 6.77 (t, *J* = 2.3 Hz, 1H), 6.56 – 6.52 (m, 1H), 5.86 (d, *J* = 1.7 Hz, 1H), 3.56 (s, 3H), 1.46 (sept, *J* = 7.4 Hz, 3H), 1.10 (d, *J* = 7.5 Hz, 18H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 170.6, 133.7, 131.2, 126.0, 125.6, 115.0, 109.4, 102.7, 56.3, 17.9, 11.7. **ESI-HRMS** calculated for $C_{18}H_{30}NO_3Si$ $(M+H)^+$: 336.1989; found: 336.1984.

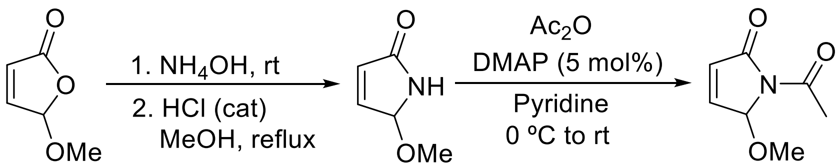
(*E*)-5-Methoxy-3-(oct-1-en-1-yl)furan-2(5H)-one (**(±)-2g**):



The reaction was carried out using (E)-oct-1-en-1-ylboronic acid (0.436 g, 2.8 mmol) following the general procedure **GP2**. Purification by flash column chromatography on Iatrobeads silica gel (Cy:EtOAc = 97:3) yielded the compound **(±)-2g** as a yellow oil (113 mg, 39% yield).

^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 6.85 (dt, *J* = 15.9, 7.0 Hz, 1H), 6.76 (d, *J* = 1.5 Hz, 1H), 6.09 (d, *J* = 15.9 Hz, 1H), 5.75 (d, *J* = 1.5 Hz, 1H), 3.54 (s, 3H), 2.22 – 2.11 (m, 2H), 1.36 – 1.20 (m, 8H), 0.91 – 0.83 (m, 3H). Spectroscopic data are in agreement with published data.[11]

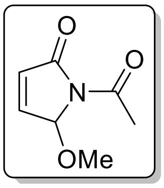
Synthesis of 1-Acetyl-5-methoxy-1*H*-pyrrol-2(5*H*)-one ((±)-2h)



5-Methoxyfuran-2(5*H*)-one (**(±)-2a**) (171 mg, 1.5 mmol) was stirred on aq. NH_3 (28%) for 1h. After completion, followed by TLC, the reaction was washed with water and extracted three times with ethyl acetate. The combined organic phases were dried over $MgSO_4$ and concentrated in vacuum.

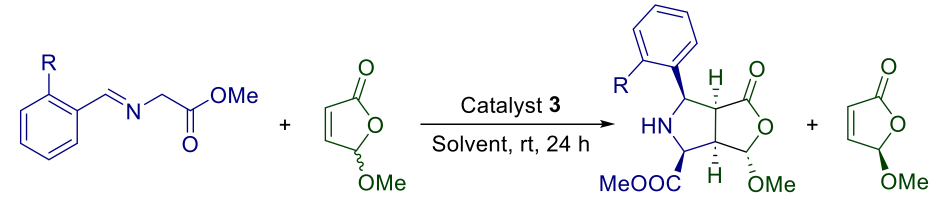
The reaction crude was dissolved in MeOH (25 mL) and 1 drop of concentrated HCl was added. The solution was stirred reflux temperature for 2h. After that, the reaction was quenched with a solution of sodium acetate in water [0.05]M and extracted with ethyl acetate three times. The organic phase was dried over $MgSO_4$ and concentrated in vacuum. The obtained product was used without further purification in the next step.

To crude 5-methoxy-1*H*-pyrrol-2(5*H*)-one was added acetic anhydride (2.4 mL, 25.4 mmol) and the resulting solution was stirred under N_2 at 0 ºC. Then, pyridine (2 equiv.) and DMAP (5 mol%) were added and the reaction was stirred at room temperature for 2h. After completion, the reaction was quenched with NH_4Cl (sat) and extracted with CH_2Cl_2. The combined organic phases were dried over $MgSO_4$ and concentrated in vacuum. Purification by flash column chromatography on Iatrobeads silica gel (Cy:EtOAc = 90:10) yielded de compound **(±)-2h** as a colourless oil (208 mg, 90% yield).

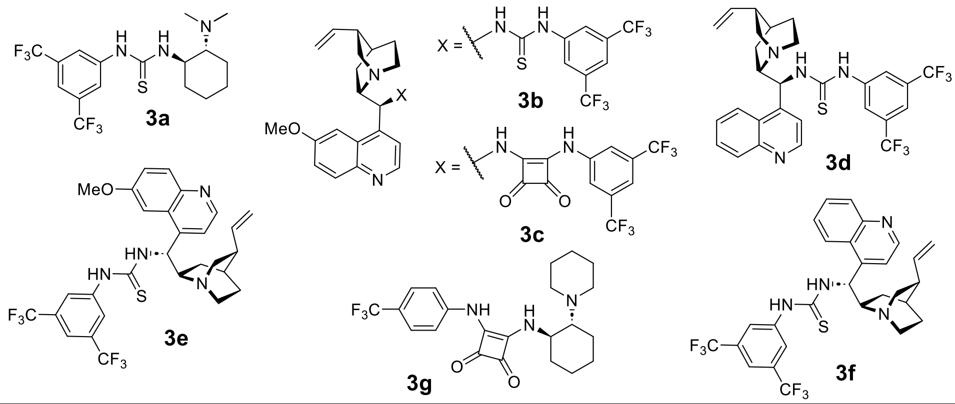


^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 7.08 (dd, *J* = 6.1, 2.0 Hz, 1H), 6.17 (dd, *J* = 6.1, 0.8 Hz, 1H), 5.99 (dd, *J* = 2.0, 0.8 Hz, 1H), 3.44 (s, 3H), 2.54 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 170.1, 168.7, 146.8, 128.1, 87.8, 55.5, 25.0. **ESI-HRMS** calculated for $C_7H_{10}NO_3$ $(M+H)^+$: 156.0656; found: 156.0654.

Screening of the Reaction Conditions



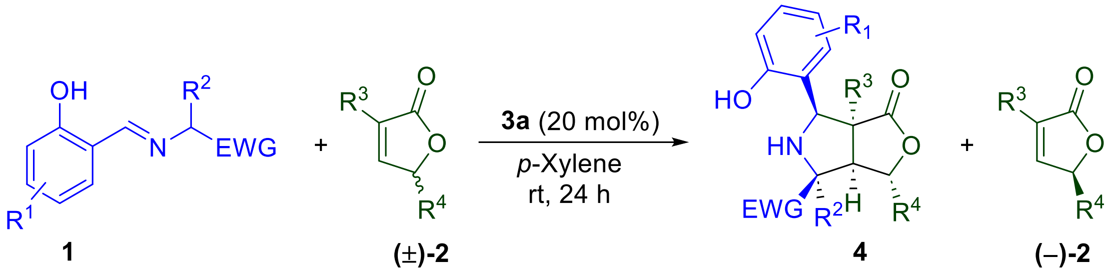
1a, R=H
1b, R=OH
(±)-**2a**
4a, R=H
4b, R=OH
(–)-**2a**



Entry[a]	Imine	Cat (mol%)	Solvent	Conv (%)[b]	*ee* 4b (%)[c]	*ee* (–)-2a (%)[c]	s (c%)[d]
1	**1a**	**3a** (20)	*p*-xylene	15	21 (**4a**)	---	---
2	**1b**	**3a (20)**	***p*-xylene**	**48**	**97**	**87**	**190 (47)**
3	**1b**	---	*p*-xylene	<5	---	---	---
4	**1b**	**3b** (20)	*p*-xylene	40	96	65	96 (40)
5	**1b**	**3c** (20)	*p*-xylene	10	---	---	---
6	**1b**	**3d** (20)	*p*-xylene	20	---	---	---
7	**1b**	**3e** (20)	*p*-xylene	18	---	---	---
8	**1b**	**3f** (20)	*p*-xylene	19	---	---	---
9	**1b**	**3g** (20)	*p*-xylene	<5	---	---	---
10	**1b**	**3a** (20)	CH_2Cl_2	34	86	50	22 (37)
11	**1b**	**3a** (20)	Et_2O	47	95	91	124 (48)
12	**1b**	**3a** (20)	MTBE	45	91	82	54 (47)
13	**1b**	**3a** (20)	Toluene	48	92	98	110 (51)
14	**1b**	**3a** (20)	Dioxane	10	---	---	---
15[e]	**1b**	**3a** (20)	*p*-xylene	45	95	81	98 (46)
16[f]	**1b**	**3a** (20)	*p*-xylene	37	95	63	74 (39)
17	**1b**	**3a** (15)	*p*-xylene	42	97	76	151 (44)
18	**1b**	**3a** (10)	*p*-xylene	38	97	55	114 (36)
19[g]	**1b**	**3a (20)**	*p*-xylene	48	97	92	>200 (49)
20[h]	**1b**	**3a** (20)	*p*-xylene	40	95	68	80 (41)

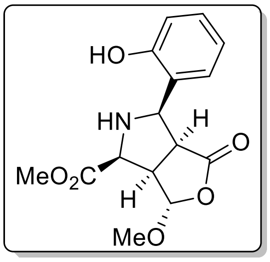
[a] The reaction was run from 0.1 mmol of imine **1** and 0.1 mmol of pseudoester **(±)-2a** in 0.3 mL of indicated solvent ([0.33]M). [b] Conversion determined by ^{1}H-NMR. [c] Determined by chiral SFC. [d] Calculated conversion (C)=$ee_{SM}/(ee_{SM}+ee_{PR})$, Selectivity factor (s)=ln[(1-C)(1-*ee*SM)]/ln[(1-C)(1+*ee*SM)]. [e] [0.16]M instead of [0.33]M. [f] [0.10]M instead of [0.33]M. [g] The reaction was scaled up to 1.0 mmol of **1**. [h] The reaction was carried out from 0.05 mmol of imine **1b**.

General Procedure (GP3) for the synthesis of compounds 4.



An oven-dried 6 mL vial equipped with a magnetic stirring bar was charged with imine **1** (1.0 equiv.), dipolarophile **(±)-2** (1.0 equiv.) and Takemoto's bifunctional organocatalyst (1-[3,5-Bis(trifluoromethyl)phenyl]-3-[(1*R*,2*R*)-(−)-2-(dimethylamino)cyclohexyl]thiourea) **3a** (20 mol%). Then, *p*-xylene (0.3 mL, [0.33]M) were added and the reaction was stirred for 24 h at room temperature. After the reaction was complete, the solvent was evaporated under reduced pressure and the residue was further purified by flash column chromatography on Iatrobeads silica gel to afford the corresponding products **4** and **(–)-2**.

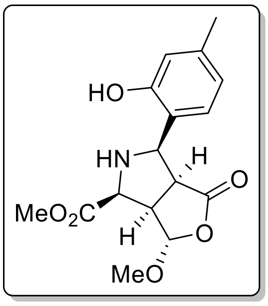
Methyl (3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(2-hydroxyphenyl)-3-methoxy-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (**4b**):



The reaction of methyl (*E*)-2-((2-hydroxybenzylidene)amino)acetate (**1b**) (19.3 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4b** as a white solid (14.4 mg, 47% yield) and **(–)-2a** as a colorless oil (4.9 mg, 43% yield).
The enantiomeric excess for **4b** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 5.71 min, τ_{major} = 6.45 min (97% *ee*). $[\alpha]^{20}_D$ = 0.315 (c = 0.4, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 0.87 min, τ_{major} = 0.74 min (87% *ee*). $[\alpha]^{20}_D$ = –0.016 (c = 0.32, $CHCl_3$). **c = 47%**, ***s* = 190** (Calculated as *s* = 188).
For 1 mmol scale up: The reaction of methyl (*E*)-2-((2-hydroxybenzylidene)amino)acetate (**1b**) (193 mg, 1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (114 mg, 1 mmol), and Takemoto's catalyst **3a** (82.6 mg, 20 mol%) in *p*-xylene (3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4b** as a white solid (146.9 mg, 47% yield) and **(–)-2a** as a colorless oil (52 mg, 46% yield). The enantiomeric excess for **4b** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 5.71 min, τ_{major} = 6.45 min (97% *ee*). $[\alpha]^{20}_D$ = 0.315 (c = 0.4, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.34 min, τ_{major} = 1.03 min (92% *ee*). **c = 49%, *s* > 200** (Calculated as *s* = 217).
^{1}H NMR (300 MHz, CD_2Cl_2) *δ*: 9.98 (brs, 1H), 7.22 (ddd, *J* = 8.1, 7.3, 1.7 Hz, 1H), 7.10 (dd, *J* = 7.5, 1.7 Hz, 1H), 6.87 (td, *J* = 7.5, 1.2 Hz, 1H), 6.80 (dd, *J* = 8.1, 1.2 Hz, 1H), 5.25 (d, *J* = 3.2 Hz, 1H), 4.60 (d, *J* = 9.3 Hz, 1H), 4.11 (d, *J* = 7.2 Hz, 1H), 3.87 (s, 3H), 3.51 (s, 3H), 3.44 (t, *J* = 9.2 Hz, 1H), 3.30 – 3.23 (m, 1H), 3.02 (brs, 1H). **^{13}C NMR**

(75 MHz, CD_2Cl_2) δ: 172.6, 169.8, 157.7, 129.6, 129.0, 119.7, 119.4, 117.0, 106.3, 64.5, 61.5, 57.5, 52.5, 48.3, 48.2. **ESI-HRMS** calculated for $C_{15}H_{18}NO_6$ $(M+H)^+$: 308,1129; found: 308.1154.

Methyl (3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(2-hydroxy-4-methylphenyl)-3-methoxy-1-oxohexahydro-1H-furo[3,4-c]pyrrole-4-carboxylate (**4c**):

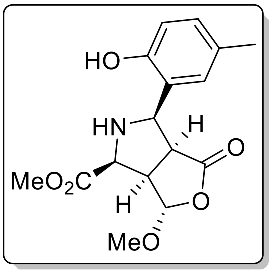


The reaction of methyl (*E*)-2-((2-hydroxy-4-methylbenzylidene)amino)acetate (**1c**) (20.7 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4c** as a white solid (13.5 mg, 42% yield) and **(–)-2a** as a colorless oil (4.7 mg, 41% yield).

The enantiomeric excess for **4c** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 4.63 min, τ_{major} = 5.21 min (99% *ee*). $[\alpha]^{20}_D$ = 0.434 (c = 0.49, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.07 min, τ_{major} = 0.85 min (90% *ee*). **c = 48%**, ***s* > 200** (Calculated as *s* = 618).

^{1}H NMR (300 MHz, CD_2Cl_2) δ: 6.93 (d, *J* = 7.7 Hz, 1H), 6.66 (d, *J* = 7.7 Hz, 1H), 6.60 (s, 1H), 5.20 (d, *J* = 3.2 Hz, 1H), 4.54 (d, *J* = 9.1 Hz, 1H), 4.07 (d, *J* = 7.1 Hz, 1H), 3.82 (s, 3H), 3.47 (s, 3H), 3.38 (t, *J* = 9.2 Hz, 1H), 3.25 – 3.18 (m, 1H), 2.27 (s, 3H). **^{13}C NMR** (75 MHz, CD_2Cl_2) δ: 172.5, 169.8, 157.5, 140.0, 128.8, 120.3, 117.7, 116.5, 106.2, 64.5, 61.6, 57.6, 52.51, 48.3, 48.3, 21.0. **ESI-HRMS** calculated for $C_{16}H_{20}NO_6$ $(M+H)^+$: 322,1285 ; found: 322.1277.

Methyl (3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(2-hydroxy-5-methylphenyl)-3-methoxy-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (**4d**):

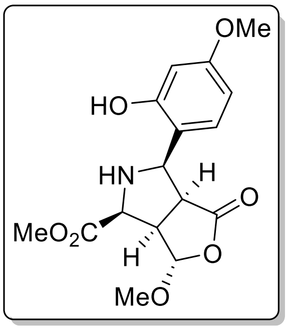


The reaction of methyl (*E*)-2-((2-hydroxy-5-methylbenzylidene)amino)acetate (**1d**) (20.7 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4d** as a white solid (15.4 mg, 48% yield) and **(–)-2a** as a colorless oil (4.7 mg, 41% yield).

The enantiomeric excess for **4d** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 5.04 min, τ_{major} = 5.71 min (98% *ee*). $[\alpha]^{20}_D$ = 0.520 (c = 0.4, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.12 min, τ_{major} = 0.87 min (86% *ee*). **c = 47%**, ***s* > 200** (Calculated as *s* = 276).

^{1}H NMR (300 MHz, CD_2Cl_2) δ: 9.63 (brs, 1H), 7.01 (dd, *J* = 8.3, 2.3 Hz, 1H), 6.88 (d, *J* = 2.2 Hz, 1H), 6.67 (d, *J* = 8.2 Hz, 1H), 5.21 (d, *J* = 3.2 Hz, 1H), 4.52 (d, *J* = 9.1 Hz, 1H), 4.08 (d, *J* = 7.1 Hz, 1H), 3.84 (s, 3H), 3.49 (s, 3H), 3.40 (t, *J* = 9.2 Hz, 1H), 3.26 – 3.20 (m, 1H), 2.94 (brs, 1H), 2.26 (s, 3H). **^{13}C NMR** (75 MHz, CD_2Cl_2) δ: 172.5, 169.84, 155.3, 130.2, 129.4, 128.6, 119.2, 116.8, 106.3, 64.7, 61.6, 57.5, 52.5, 48.3, 48.2, 20.2. **ESI-HRMS** calculated for $C_{16}H_{20}NO_6$ $(M+H)^+$: 322,1285; found: 322.1261.

Methyl (3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(2-hydroxy-4-methoxyphenyl)-3-methoxy-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (**4e**):

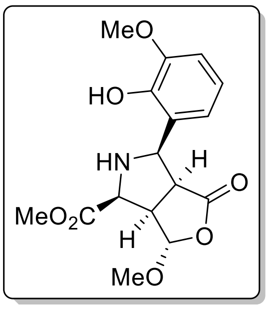


The reaction of methyl (*E*)-2-((2-hydroxy-4-methoxybenzylidene)amino)acetate (**1e**) (22.3 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4e** as a white solid (15.8 mg, 47% yield) and **(–)-2a** as a colorless oil (5.1 mg, 45% yield).

The enantiomeric excess for **4e** was determined by SFC on a *Daicel Chiralpak* IB-3 column: CO_2/MeOH gradient from 95:5 to 60:30 in 8 min, flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 4.12 min, τ_{major} = 4.37 min (97% *ee*). $[\alpha]^{20}_{D}$ = 0.538 (c = 0.36, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.07 min, τ_{major} = 0.85 min (90% *ee*). **c = 48%**, ***s* > 200** (Calculated as *s* = 204).

^{1}H NMR (300 MHz, CD_3CN) *δ*: 10.44 (brs, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.35 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.25 (d, *J* = 2.6 Hz, 1H), 5.17 (d, *J* = 3.3 Hz, 1H), 4.55 (d, *J* = 9.3 Hz, 1H), 4.05 (d, *J* = 7.2 Hz, 1H), 3.77 (s, 3H), 3.71 (s, 3H), 3.43 (s, 3H), 3.41 (t, *J* = 9.2 Hz, 1H), 3.58 – 3.26 (brs, 1H), 3.19 – 3.13 (m, 1H). **^{13}C NMR** (75 MHz, CD_3CN) *δ*: 174.0, 171.4, 161.64, 159.9, 130.7, 114.2, 107.2, 105.3, 102.8, 64.2, 62.0, 57.9, 55.8, 53.0, 49.3, 49.0. **ESI-HRMS** calculated for $C_{16}H_{20}NO_7$ $(M+H)^+$: 338,1234; found: 338.1252.

Methyl (3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(2-hydroxy-3-methoxyphenyl)-3-methoxy-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (**4f**):

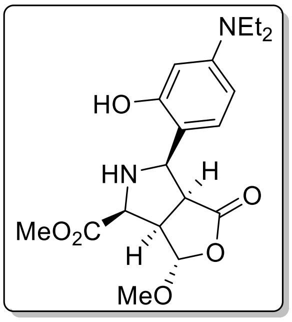


The reaction of methyl (*E*)-2-((2-hydroxy-3-methoxybenzylidene)amino)acetate (**1f**) (22.3 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4f** as a white solid (16.2 mg, 48% yield) and **(–)-2a** as a colorless oil (5.0 mg, 44% yield).

The enantiomeric excess for **4f** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 5.31 min, τ_{major} = 5.57 min (94% *ee*). $[\alpha]^{20}_{D}$ = 0.525 (c = 0.36, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.17 min, τ_{major} = 0.91 min (86% *ee*). **c = 48%**, ***s* = 90.**

^{1}H NMR (300 MHz, CD_3CN) *δ*: 8.62 (brs, 1H), 6.99 – 6.61 (m, 3H), 5.16 (d, *J* = 3.1 Hz, 1H), 4.59 (d, *J* = 8.9 Hz, 1H), 4.05 (d, *J* = 7.2 Hz, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 3.48 (t, *J* = 9.0 Hz, 1H), 3.15 (ddd, *J* = 9.1, 7.0, 3.1 Hz, 1H), 3.08 (s, 1H). **^{13}C NMR** (76 MHz, CD_3CN) *δ*: 174.3, 171.7, 148.4, 146.5, 123.8, 120.9, 119.9, 112.1, 107.4, 62.3, 62.1, 57.9, 56.6, 52.9, 49.6, 48.6. **ESI-HRMS** calculated for $C_{16}H_{20}NO_7$ $(M+H)^+$: 338,1234; found: 338.1216.

Methyl (3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(4-(diethylamino)-2-hydroxyphenyl)-3-methoxy-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (**4g**):

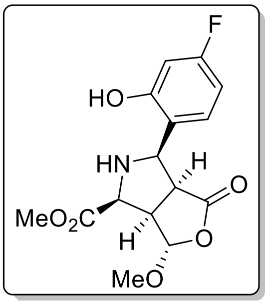


The reaction of methyl (*E*)-2-((2-hydroxybenzylidene)amino)acetate (**1g**) (19.32 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4g** as a white solid (11.5 mg, 30% yield) and **(–)-2a** as a colorless oil (6.8 mg, 60% yield).

The enantiomeric excess for **4g** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 5.10 min, τ_{major} = 5.69 min (98% *ee*). $[\alpha]^{20}_D$ = 0.230 (c = 0.22, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.23 min, τ_{major} = 0.95 min (34% *ee*). **c = 25%**, ***s* = 170.**

^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.85 (d, *J* = 8.2 Hz, 1H), 6.26 – 6.10 (m, 2H), 5.26 (d, *J* = 3.3 Hz, 1H), 4.51 (d, *J* = 9.2 Hz, 1H), 4.03 (d, *J* = 6.8 Hz, 1H), 3.84 (s, 3H), 3.50 (s, 3H), 3.36 (t, *J* = 9.2 Hz, 1H), 3.30 (q, *J* = 7.0 Hz, 4H), 3.20 (ddd, *J* = 9.6, 6.8, 3.3 Hz, 1H), 1.14 (t, *J* = 7.0 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 172.6, 169.8, 158.6, 149.7, 129.7, 106.3, 105.7, 103.8, 100.4, 65.0, 61.6, 57.8, 52.6, 48.6, 48.4, 44.4, 12.8. **ESI-HRMS** calculated for $C_{19}H_{27}N_2O_6$ $(M+H)^+$: 379,1838; found: 379.1834.

Methyl (3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(4-fluoro-2-hydroxyphenyl)-3-methoxy-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (**4h**):

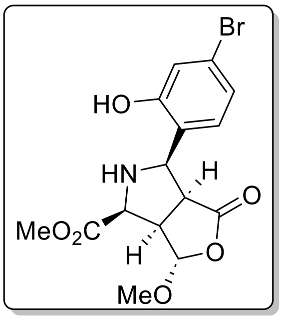


The reaction of methyl (*E*)-2-((4-fluoro-2-hydroxybenzylidene)amino)acetate (**1h**) (21.1 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4h** as a white solid (14.6 mg, 45% yield) and **(–)-2a** as a colorless oil (5.0 mg, 44% yield).

The enantiomeric excess for **4h** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 4.37 min, τ_{major} = 5.00 min (82% *ee*). $[\alpha]^{20}_D$ = 0.325 (c = 0.53, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.19 min, τ_{major} = 0.92 min (87% *ee*). **c = 51%**, ***s* = 28.**

^{1}H NMR (300 MHz, CD_3CN) δ: 10.83 (brs, 1H), 7.09 (dd, *J* = 8.6, 6.7 Hz, 1H), 6.54 (td, *J* = 8.6, 2.6 Hz, 1H), 6.46 (dd, *J* = 10.8, 2.6 Hz, 1H), 5.18 (d, *J* = 3.2 Hz, 1H), 4.62 (d, *J* = 9.3 Hz, 1H), 4.09 (d, *J* = 7.4 Hz, 1H), 3.78 (s, 3H), 3.47 (t, *J* = 9.3 Hz, 1H), 3.44 (s, 3H), 3.19 (ddd, *J* = 9.2, 7.4, 3.2 Hz, 1H). **^{13}C NMR** (75 MHz, CD_3CN) δ: 174.0, 171.3, 164.2 (d, *J* = 242.3), 160.3 (d, *J* = 12.4 Hz), 131.1 (d, *J* = 10.5 Hz), 107.2, 106.5 (d, *J* = 21.8 Hz), 104.3 (d, *J* = 24.2 Hz), 63.9, 62.0, 58.0, 53.0, 49.2, 48.9. **^{19}F NMR** (471 MHz, CD_3CN) δ: -115.4. **ESI-HRMS** calculated for $C_{15}H_{17}FNO_6$ $(M+H)^+$: 326,1034; found: 326.1058.

Methyl (3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(4-bromo-2-hydroxyphenyl)-3-methoxy-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (**4i**):

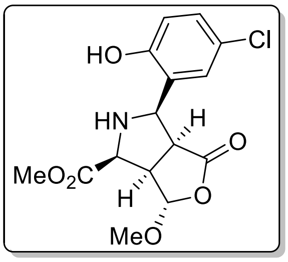


The reaction of methyl (*E*)-2-((4-bromo-2-hydroxybenzylidene)amino)acetate (**1i**) (27.2 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4i** as a white solid (15.4 mg, 40% yield) and **(–)-2a** as a colorless oil (5.0 mg, 44% yield).

The enantiomeric excess for **4i** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 7.13 min, τ_{major} = 7.65 min (95% *ee*). $[\alpha]^{20}_D$ = 0.495 (c = 0.4, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.22 min, τ_{major} = 0.94 min (68% *ee*). **c = 41%**, ***s* = 80.**

^{1}H NMR (300 MHz, $(CD_3)_2SO$) *δ*: 10.30 (s, 1H), 7.18 (d, *J* = 7.9 Hz, 1H), 6.94 – 6.88 (m, 2H), 5.06 (d, *J* = 2.8 Hz, 1H), 4.42 (dd, *J* = 8.5, 4.5 Hz, 1H), 4.00 (dd, *J* = 6.9, 4.7 Hz, 1H), 3.74 (s, 3H), 3.61 – 3.53 (m, 1H), 3.49 (t, *J* = 8.6 Hz, 1H), 3.36 (s, 3H), 3.18 – 3.04 (m, 1H). **^{13}C NMR** (75 MHz, $(CD_3)_2SO$) *δ*: 173.3, 170.7, 156.3, 128.9, 124.3, 121.2, 120.1, 117.1, 106.0, 61.0, 58.6, 56.7, 51.9, 48.1, 46.6. **ESI-HRMS** calculated for $C_{15}H_{17}BrNO_6$ $(M+H)^+$: 386,0234 and 388,0214; found: 386.0250 and 388.0231.

Methyl (3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(5-chloro-2-hydroxyphenyl)-3-methoxy-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (**4j**):

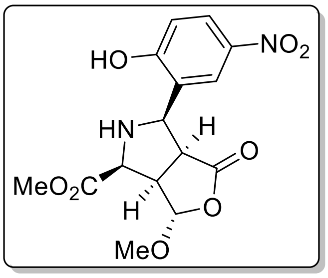


The reaction of methyl (*E*)-2-((5-chloro-2-hydroxybenzylidene)amino)acetate (**1j**) (22.7 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4j** as a white solid (12.6 mg, 35% yield) and **(–)-2a** as a colorless oil (4.4 mg, 39% yield).

The enantiomeric excess for **4j** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 7.06 min, τ_{major} = 7.43 min (93% *ee*). $[\alpha]^{20}_D$ = 0.355 (c = 0.32, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.19 min, τ_{major} = 0.92 min (56% *ee*). **c = 37%**, ***s* = 49.**

^{1}H NMR (300 MHz, CD_3CN) *δ*: 10.29 (brs, 1H), 7.17 – 7.08 (m, 2H), 6.69 (d, *J* = 8.4 Hz, 1H), 5.18 (d, *J* = 3.2 Hz, 1H), 4.58 (d, *J* = 9.2 Hz, 1H), 4.10 (d, *J* = 7.3 Hz, 1H), 3.79 (s, 3H), 3.51 (t, *J* = 9.2 Hz, 1H), 3.44 (s, 3H), 3.19 (ddd, *J* = 9.0, 7.2, 3.1 Hz, 1H). **^{13}C NMR** (75 MHz, CD_2Cl_2) *δ*: 172.3, 169.6, 156.5, 129.5, 128.5, 123.9, 121.3, 118.6, 106.2, 67.8, 64.0, 61.6, 57.6, 52.6, 48.2. **ESI-HRMS** calculated for $C_{15}H_{17}ClNO_6$ $(M+H)^+$: 342.0739 and 344.0710; found: 342.0763 and 344.0759.

Methyl (3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(2-hydroxy-5-nitrophenyl)-3-methoxy-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (4k):

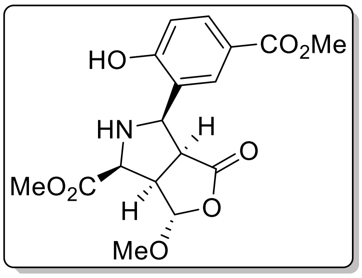


The reaction of methyl (*E*)-2-((2-hydroxy-5-nitrobenzylidene)amino)acetate (**1k**) (23.8 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4k** as a white solid (16.5 mg, 47% yield) and **(–)-2a** as a colorless oil (4.6 mg, 40% yield).

The enantiomeric excess for **4k** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 7.01 min, τ_{major} = 7.26 min (95% *ee*). $[\alpha]^{20}_D$ = 0.450 (c = 0.65, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.17 min, τ_{major} = 0.91 min (90% *ee*). **c = 49%**, ***s* = 120.**

^{1}H NMR (300 MHz, CD_3CN) *δ*: 11.55 (brs, 1H), 8.09 (d, *J* = 2.8 Hz, 1H), 8.05 (dd, *J* = 8.9, 2.8 Hz, 1H), 6.84 (d, *J* = 8.9 Hz, 1H), 5.19 (d, *J* = 2.9 Hz, 1H), 4.74 (d, *J* = 9.1 Hz, 1H), 4.17 (d, *J* = 7.7 Hz, 1H), 3.80 (s, 3H), 3.60 (t, *J* = 9.2 Hz, 1H), 3.44 (s, 3H), 3.24 (ddd, *J* = 9.2, 7.7, 3.0 Hz, 1H). **^{13}C NMR** (75 MHz, CD_3CN) *δ*: 174.0, 171.3, 164.9, 141.2, 126.2, 125.8, 123.3, 117.7, 107.2, 63.1, 62.1, 58.0, 53.1, 49.0, 48.7. **ESI-HRMS** calculated for $C_{15}H_{17}N_2O_8$ $(M+H)^+$: 353,0979; found: 353.0991.

Methyl (3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(2-hydroxy-5-(methoxycarbonyl)phenyl)-3-methoxy-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (4l):

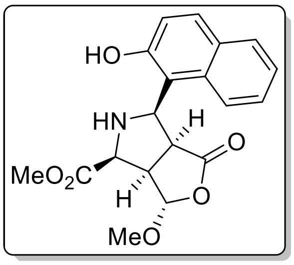


The reaction of methyl (*E*)-4-hydroxy-3-(((2-methoxy-2-oxoethyl)imino) methyl)benzoate (**1l**) (25.1 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4l** as a white solid (12.8 mg, 35% yield) and **(–)-2a** as a colorless oil (6.2 mg, 54% yield).

The enantiomeric excess for **4l** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 5.08 min, τ_{major} = 5.54 min (91% *ee*). $[\alpha]^{20}_D$ = 0.450 (c = 0.65, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.26 min, τ_{major} = 0.97 min (56% *ee*). **c = 38%**, ***s* = 37**.

^{1}H NMR (300 MHz, $(CD_3)_2SO$) *δ*: 10.74 (s, 1H), 7.91 (d, *J* = 2.3 Hz, 1H), 7.72 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 5.08 (d, *J* = 2.6 Hz, 1H), 4.46 (dd, *J* = 8.4, 3.5 Hz, 1H), 4.03 (dd, *J* = 7.1, 3.9 Hz, 1H), 3.79 (s, 3H), 3.76 (s, 3H), 3.65 – 3.58 (m, 1H), 3.54 (t, *J* = 8.6 Hz, 1H), 3.36 (s, 3H), 3.12 (ddd, *J* = 9.2, 6.9, 2.6 Hz, 1H). **^{13}C NMR** (75 MHz, $(CD_3)_2SO$) *δ*: 173.4, 170.8, 166.3, 159.8, 130.0, 128.6, 125.1, 119.8, 114.5, 106.1, 61.1, 58.6, 56.6, 51.9, 51.5, 47.9, 46.5. **ESI-HRMS** calculated for $C_{17}H_{20}NO_8$ $(M+H)^+$: 366,1183; found: 366.1159.

Methyl (3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(2-hydroxynaphthalen-1-yl)-3-methoxy-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (4m):

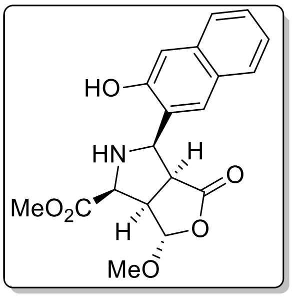


The reaction of methyl (*E*)-2-(((2-hydroxynaphthalen-1-yl)methylene)amino)acetate (**1m**) (24.3 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3**, but at 50 ºC for two days, and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4m** as an orange solid (16.4 mg, 46% yield) and **(–)-2a** as a colorless oil (5.1 mg, 45% yield).

The enantiomeric excess for **4m** was determined by SFC on a *Daicel Chiralpak* IB-3 column: CO_2/MeOH gradient from 95:5 to 70:30 in 8 min, flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 6.05 min, τ_{major} = 6.47 min (93% *ee*). $[\alpha]^{20}_D$ = 0.152 (c = 0.2, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.12, τ_{major} = 0.94 min (91% *ee*). **c = 50%**, ***s* = 88**.

^{1}H NMR (300 MHz, CD_3CN) *δ*: 12.1 (brs, 1H) 7.94 – 7.64 (m, 3H), 7.56 – 7.42 (m, 1H), 7.41 – 7.23 (m, 1H), 6.95 (d, *J* = 8.9 Hz, 1H), 5.41 (d, *J* = 9.5 Hz, 1H), 5.28 (d, *J* = 3.4 Hz, 1H), 4.21 (d, *J* = 7.6 Hz, 1H), 3.81 (s, 3H), 3.73 (t, *J* = 9.4 Hz, 1H), 3.45 (s, 3H), 3.37 – 3.25 (m, 1H). **^{13}C NMR** (75 MHz, CD_3CN) *δ*: 173.7, 171.3, 157.9, 133.7, 130.8, 129.7, 129.3, 127.8, 123.7, 122.2, 120.8, 111.6, 107.2, 62.0, 60.8, 58.0, 53.1, 49.5, 48.1. **ESI-HRMS** calculated for $C_{19}H_{20}NO_6$ $(M+H)^+$: 358,1285; found: 358.1299.

Methyl (3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(3-hydroxynaphthalen-2-yl)-3-methoxy-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (4n):

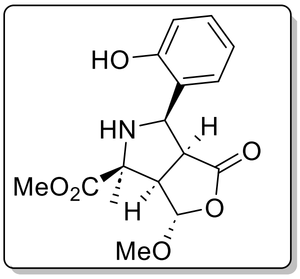


The reaction of methyl (*E*)-2-(((3-hydroxynaphthalen-2-yl)methylene)amino)acetate (**1n**) (24.3 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3**, but at 50 ºC for two days, and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4n** as an orange solid (11.8 mg, 33% yield) and **(–)-2a** as a colorless oil (5.6 mg, 49% yield).

The enantiomeric excess for **4n** was determined by SFC on a *Daicel Chiralpak* IB-3 column: CO_2/MeOH gradient from 95:5 to 70:30 in 8 min, flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 6.09 min, τ_{major} = 6.49 min (97% *ee*). $[\alpha]^{20}_D$ = 0.187 (c = 0.2, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.20, τ_{major} = 0.93 min (33% *ee*). **c = 25%**, ***s* = 91**.

^{1}H NMR (300 MHz, CD_3CN) *δ*: 12.11 (brs, 1H), 7.87 – 7.74 (m, 2H), 7.70 (d, *J* = 8.9 Hz, 1H), 7.49 (dd, *J* = 8.6, 6.9 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 6.97 (dd, *J* = 8.9, 1.8 Hz, 1H), 5.43 (d, *J* = 9.5 Hz, 1H), 5.29 (d, *J* = 3.3Hz, 1H), 4.22 (d, *J* = 7.3 Hz, 1H), 3.82 (s, 3H), 3.75 (t, *J* = 9.4 Hz, 1H), 3.46 (s, 3H), 3.33 – 3.26 (m, 1H). **^{13}C NMR** (75 MHz, CD_3CN) *δ*: 173.7, 171.3, 157.9, 133.7, 130.8, 129.6, 129.3, 127.8, 123.7, 122.1, 120.8, 111.5, 107.2, 62.0, 60.8, 58.4, 53.1, 49.5, 48.1. **ESI-HRMS** calculated for $C_{19}H_{20}NO_6$ $(M+H)^+$: 358,1285; found: 358.1273.

Methyl (3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(2-hydroxyphenyl)-3-methoxy-4-methyl-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (4o):

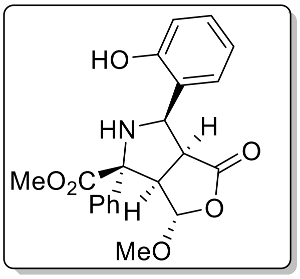


The reaction of methyl (*E*)-2-((2-hydroxybenzylidene)amino)propanoate (**1o**) (20.7 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4o** as a white solid (14.8 mg, 46% yield) and **(–)-2a** as a colorless oil (5.3 mg, 47% yield).

The enantiomeric excess for **4o** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 4.01 min, τ_{major} = 4.97 min (87% *ee*). $[\alpha]^{20}_{D}$ = 0.523 (c = 0.47, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.19 min, τ_{major} = 0.94 min (91% *ee*). **c = 51%**, ***s* = 45**.

^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 7.20 (td, *J* = 7.7, 1.7 Hz, 1H), 7.04 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.88 – 6.80 (m, 2H), 5.19 (d, *J* = 3.8 Hz, 1H), 4.85 (d, *J* = 9.6 Hz, 1H), 3.84 (s, 3H), 3.57–3.47 (m, 1H), 3.49 (s, 3H), 2.94 (dd, *J* = 9.1, 3.6 Hz, 1H), 1.58 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: δ 172.7, 172.2, 157.7, 130.2, 129.2, 119.9, 119.4, 117.8, 107.1, 67.4, 62.4, 58.1, 55.6, 53.0, 48.4, 24.6. **ESI-HRMS** calculated for $C_{16}H_{20}NO_6$ $(M+H)^+$: 322,1285; found: 322.1299.

Methyl (3*S*,3a*R*,4*R*,6*R*,6a*S*)-6-(2-hydroxyphenyl)-3-methoxy-1-oxo-4-phenylhexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (4p):

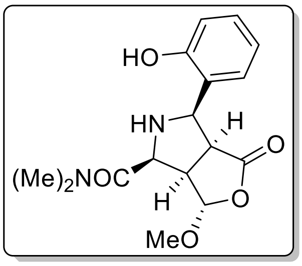


The reaction of methyl (*E*)-2-((2-hydroxybenzylidene)amino)-2-phenylacetate (**1p**) (26.9 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4p** as a white solid (13.8 mg, 36% yield) and **(–)-2a** as a colorless oil (5.5 mg, 48% yield).

The enantiomeric excess for **4p** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 3.60 min, τ_{major} = 3.87 min (71% *ee*). $[\alpha]^{20}_{D}$ = 0.195 (c = 0.4, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.21 min, τ_{major} = 0.93min (65% *ee*). **c = 48%**, ***s* = 11**.

^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 9.72 (brs, 1H), 7.48 – 7.44 (m, 5H), 7.19 (t, *J* = 7.8 Hz, 1H), 6.97 (d, *J* = 7.4 Hz, 1H), 6.89 – 6.78 (m, 2H), 5.35 (d, *J* = 3.6 Hz, 1H), 4.41 (d, *J* = 9.7 Hz, 1H), 3.77 (s, 3H), 3.69 (dd, *J* = 8.9, 3.6 Hz, 1H), 3.58 (s, 3H), 3.46 – 3.34 (m, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 172.5, 170.9, 157.2, 137.6, 130.1, 129.6, 129.2, 129.1, 125.4, 119.9, 119.4, 117.6, 107.7, 73.3, 61.7, 58.2, 53.7, 53.1, 48.8. **ESI-HRMS** calculated for $C_{21}H_{22}NO_6$ $(M+H)^+$: 384,1442; found: 384.1472.

(3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(2-hydroxyphenyl)-3-methoxy-*N*,*N*-dimethyl-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxamide (4q):

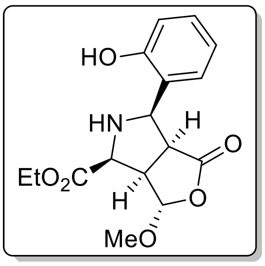


The reaction of (*E*)-2-((2-hydroxybenzylidene)amino)-*N*,*N*-dimethylacetamide (**1q**) (20.6 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4q** as a white solid (14.1 mg, 44% yield) and **(–)-2a** as a colorless oil (5.2 mg, 46% yield).

The enantiomeric excess for **4q** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 4.48 min, τ_{major} = 4.97 min (84% *ee*). $[\alpha]^{20}_D$ = 0.154 (c = 0.32, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.26 min, τ_{major} = 0.96 min (82% *ee*). **c = 49%**, ***s* = 29**.

^{1}H NMR (300 MHz, $(CD_3)_2SO$) *δ*: 10.24 (s, 1H), 7.20 – 6.94 (m, 2H), 6.78 – 6.69 (m, 2H), 5.06 (d, *J* = 3.2 Hz, 1H), 4.41 (t, *J* = 8.9 Hz, 1H), 4.22 (t, *J* = 7.3 Hz, 1H), 3.63 – 3.54 (m, 1H), 3.49 (t, *J* = 8.9 Hz, 1H), 3.34 (s, 3H), 3.27 – 3.18 (m, 1H), 3.06 (s, 3H), 2.93 (s, 3H). **^{13}C NMR** (75 MHz, $(CD_3)_2SO$) *δ*: 173.6, 168.9, 155.9, 128.2 (2C), 122.9, 118.5, 115.2, 105.4, 61.9, 59.8, 56.9, 49.4, 49.1, 35.9, 35.2. **ESI-HRMS** calculated for $C_{16}H_{21}N_2O_5$ $(M+H)^+$: 321,1445; found: 321.1439.

Ethyl (3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(2-hydroxyphenyl)-3-methoxy-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (4r):

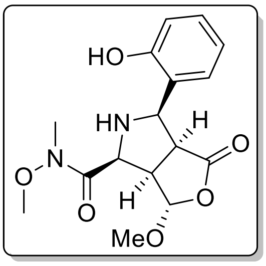


The reaction of ethyl (*E*)-2-((2-hydroxybenzylidene)amino)acetate (**1r**) (20.7 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4r** as a white solid (15.1 mg, 47% yield) and **(–)-2a** as a colorless oil (5.0 mg, 44% yield).

The enantiomeric excess for **4r** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 4.94 min, τ_{major} = 5.65 min (93% *ee*). $[\alpha]^{20}_D$ = 0.383 (c = 0.37, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.23 min, τ_{major} = 0.95 min (87% *ee*). **c = 48%**, ***s* = 80**.

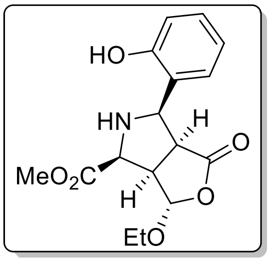
^{1}H NMR (300 MHz, CD_2Cl_2) *δ*: 9.92 (brs, 1H), 7.19 (ddd, *J* = 8.0, 7.3, 1.7 Hz, 1H), 7.06 (dd, *J* = 7.6, 1.8 Hz, 1H), 6.83 (td, *J* = 7.4, 1.2 Hz, 1H), 6.77 (dd, *J* = 8.1, 1.3 Hz, 1H), 5.23 (d, *J* = 3.2 Hz, 1H), 4.57 (d, *J* = 9.1 Hz, 1H), 4.43 – 4.18 (m, 2H), 4.06 (d, *J* = 7.1 Hz, 1H), 3.48 (s, 3H), 3.41 (t, *J* = 9.3 Hz, 1H), 3.23 (ddd, *J* = 9.2, 7.1, 3.2 Hz, 1H), 2.98 (brs, 1H), 1.33 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (75 MHz, CD_2Cl_2) *δ*: 172.9, 169.6, 158.1, 130.1, 129.4, 119.9, 119.7, 117.5, 106.6, 64.99, 62.2, 62.1, 57.8, 48.7, 48.6, 14.4. **ESI-HRMS** calculated for $C_{16}H_{20}NO_6$ $(M+H)^+$: 322,1285; found: 322.1267.

(3*S*,3a*R*,4*S*,6*R*,6a*S*)-6-(2-hydroxyphenyl)-*N*,3-dimethoxy-*N*-methyl-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxamide (**4s**)**:**



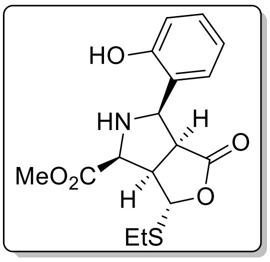
The reaction of ((*E*)-2-((2-hydroxybenzylidene)amino)-*N*-methoxy-*N*-methylacetamide (**1s**) (22.2 mg, 0.1 mmol), 5-methoxy-2(5*H*)-furanone (**(±)-2a**) (11.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4s** as a white solid (16.1 mg, 48% yield) and **(–)-2a** as a colorless oil (5.2 mg, 46% yield).
The enantiomeric excess for **4s** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 5.27 min, τ_{major} = 5.69 min (90% *ee*). $[\alpha]^{20}_D$ = 0.160 (c = 0.32, $CHCl_3$). The enantiomeric excess for **(–)-2a** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = not detected, τ_{major} = 0.93 min (>99% *ee*). **c = 52%**, ***s* = 100**.
^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 7.24 – 7.16 (m, 1H), 7.08 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.91 – 6.79 (m, 2H), 5.33 (d, *J* = 3.5 Hz, 1H), 4.63 (d, *J* = 9.4 Hz, 1H), 4.30 (d, *J* = 6.6 Hz, 1H), 3.79 (s, 3H), 3.53 – 3.44 (m, 1H), 3.49 (s, 3H), 3.34 – 3.28 (m, 1H), 3.26 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 172.6, 157.6, 130.0, 128.9, 119.7, 119.6, 117.8, 105.9, 64.2, 61.8, 60.6, 57.9, 45.0, 48.5, 32.7. **ESI-HRMS** calculated for $C_{16}H_{21}N_2O_6$ $(M+H)^+$: 337,1394; found: 337.1378.

Methyl (3*S*,3a*R*,4*S*,6*R*,6a*S*)-3-ethoxy-6-(2-hydroxyphenyl)-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (4t):



The reaction of methyl (*E*)-2-((2-hydroxybenzylidene)amino)acetate (**1b**) (19.3 mg, 0.1 mmol), 5-ethoxyfuran-2(5*H*)-one (**(±)-2b**) (12.8 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4t** as a white solid (14.4 mg, 45% yield) and **(–)-2b** as a colorless oil (4.7 mg, 37% yield). The enantiomeric excess for **4t** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 5.07 min, τ_{major} = 5.89 min (97% *ee*). $[\alpha]^{20}_D$ = 0.573 (c = 0.5, $CHCl_3$). The enantiomeric excess for **(–)-2b** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{major} = 0.82 min (>99% *ee*). $[\alpha]^{20}_D$ = – 0.018 (c = 0.34, $CHCl_3$). **c = 50%**, ***s* > 200** (Calculated as *s* = 348).
^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 9.77 (brs, 1H), 7.19 (td, *J* = 7.7, 1.7 Hz, 1H), 7.04 (dd, *J* = 7.5, 1.7 Hz, 1H), 6.83 (t, *J* = 8.6 Hz, 2H), 5.36 (d, *J* = 3.4 Hz, 1H), 4.58 (d, *J* = 9.3 Hz, 1H), 4.06 (d, *J* = 6.8 Hz, 1H), 3.90 – 3.79 (m, 4H), 3.59 (dq, *J* = 10.0, 7.0 Hz, 1H), 3.43 (t, *J* = 9.3 Hz, 1H), 3.22 (ddd, *J* = 9.6, 6.8, 3.5 Hz, 1H), 1.21 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 172.6, 169.8, 157.4, 130.0, 128.9, 119.8, 119.4, 117.5, 104.9, 66.3, 64.6, 61.7, 52.6, 48.6, 48.5, 15.0. **ESI-HRMS** calculated for $C_{16}H_{20}NO_6$ $(M+H)^+$: 322.1285; found: 322.1290.

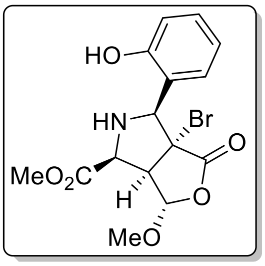
Methyl (3*R*,3a*R*,4*S*,6*R*,6a*S*)-3-(ethylthio)-6-(2-hydroxyphenyl)-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (4u):



The reaction of methyl (*E*)-2-((2-hydroxybenzylidene)amino)acetate (**1b**) (19.3 mg, 0.1 mmol), 5-(ethylthio)furan-2(5*H*)-one (**(±)-2c**) (14.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4u** as a white solid (9 mg, 26% yield) and **(–)-2c** as a colorless oil (4.3 mg, 29% yield). The enantiomeric excess for **4u** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 4.89 min, τ_{major} = 5.31 min (92% *ee*). $[\alpha]^{20}_D$ = 0.533 (c = 0.33, $CHCl_3$). The enantiomeric excess for **(–)-2c** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.24 min, τ_{major} = 1.63 min (1% *ee*). **c = n.d.**, ***s* = n.d.**

^{1}H NMR (300 MHz, $CDCl_3$) *δ:* 7.22 (t, *J* = 7.8 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.87 (t, *J* = 6.8 Hz, 2H), 5.58 (d, *J* = 6.8 Hz, 1H), 4.68 (d, *J* = 9.8 Hz, 1H), 4.10 (d, *J* = 6.1 Hz, 1H), 3.84 (s, 3H), 3.45 (t, *J* = 9.6 Hz, 1H), 3.22 (dt, *J* = 9.4, 6.5 Hz, 1H), 2.87 – 2.62 (m, 2H), 1.31 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 172.8, 169.5, 157.3, 130.3, 129.0, 120.0, 119.2, 117.8, 84.7, 64.7, 62.0, 52.6, 48.8, 48.4, 26.5, 15.1. **ESI-HRMS** calculated for $C_{16}H_{20}NO_5S$ $(M+H)^+$: 338.1057; found: 338.1063.

Methyl (3*S*,3a*R*,4*S*,6*S*,6a*R*)-6a-bromo-6-(2-hydroxyphenyl)-3-methoxy-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (**4v**)**:**

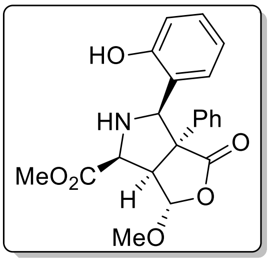


The reaction of methyl (*E*)-2-((2-hydroxybenzylidene)amino)acetate **1b** (19.3 mg, 0.1 mmol), 3-bromo-5-methoxyfuran-2(5*H*)-one (**(±)-2d**) (19.2 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4v** as a white solid (13.1 mg, 34% yield) and **(–)-2d** as a colorless oil (5.9 mg, 52% yield).

The enantiomeric excess for **4v** was determined by SFC on a *Daicel Chiralpak* IC column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 6.05 min, τ_{major} = 5.49 min (87% *ee*). $[\alpha]^{20}_D$ = 0.243 (c = 0.64, $CHCl_3$). The enantiomeric excess for **(–)-2d** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH gradient 95:5 in 8 min, flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 1.44, τ_{major} = 1.18 min (47% *ee*). $[\alpha]^{20}_D$ = -0.068 (c = 0.24, $CHCl_3$). **c = 35%**, ***s* = 22**.

^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 9.40 (brs, 1H), 7.30 – 7.16 (m, 2H), 6.93 – 6.80 (m, 2H), 5.29 (d, *J* = 3.3 Hz, 1H), 4.86 (s, 1H), 4.34 (d, *J* = 6.5 Hz, 1H), 3.86 (s, 3H), 3.53 (s, 3H), 3.44 (dd, *J* = 6.6, 3.3 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 169.1, 168.9, 157.0, 131.0, 129.8, 120.2, 117.9, 116.7, 104.6, 76.3, 60.4, 59.0, 58.8, 58.1, 53.0. **ESI-HRMS** calculated for $C_{15}H_{17}BrNO_6$ $(M+H)^+$: 386.0234 and 388.0214; found: 386.0242 and 388.0222.

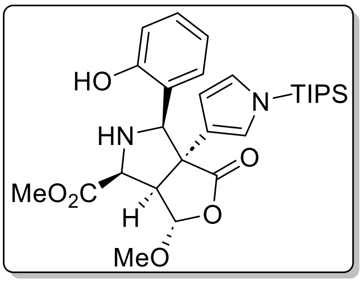
Methyl (3*S*,3a*R*,4*S*,6*S*,6a*R*)-6-(2-hydroxyphenyl)-3-methoxy-1-oxo-6a-phenylhexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (4w):



The reaction of methyl (*E*)-2-((2-hydroxybenzylidene)amino)acetate (**1b**) (19.3 mg, 0.1 mmol), 5-methoxy-3-phenylfuran-2(5*H*)-one (**(±)-2e**) (19 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in Toluene (0.3 mL, [0.33]M) at 0ºC following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4w** as a white solid (15.3 mg, 40% yield) and **(–)-2e** as a colorless oil (6.84 mg, 36% yield). The enantiomeric excess for **4w** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 4.86 min, τ_{major} = 5.04 min (75% *ee*). $[\alpha]^{20}_D$ = 0.124 (c = 0.4, $CHCl_3$). The enantiomeric excess for **(–)-2e** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm , τ_{minor} = 2.66 min, τ_{major} = 2.32 min (95% *ee*). $[\alpha]^{20}_D$ = – 0.017 (c = 0.28, $CHCl_3$). **c = 55%**, ***s* = 25**.

^{1}H NMR (300 MHz, $CDCl_3$) *δ:* 9.79 (brs, 1H), 7.56 – 7.50 (m, 2H), 7.43 – 7.29 (m, 3H), 7.25 – 7.16 (m, 2H), 6.85 (dd, *J* = 8.1, 1.2 Hz, 1H), 6.72 (td, *J* = 7.4, 1.2 Hz, 1H), 6.58 (dd, *J* = 7.6, 1.8 Hz, 1H), 5.26 (d, *J* = 2.6 Hz, 1H), 4.50 (s, 1H), 4.36 (d, *J* = 7.2 Hz, 1H), 3.87 (s, 3H), 3.59 (dd, *J* = 7.2, 2.6 Hz, 1H), 3.45 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 172.7, 169.6, 157.9, 137.9, 130.3, 129.6, 129.1, 128.1, 126.7, 119.3, 118.5, 117.6, 104.0, 75.7, 61.9, 60.8, 57.5, 55.5, 52.8. **ESI-HRMS** calculated for $C_{21}H_{22}NO_6$ $(M+H)^+$: 384.1442; found: 384.1448.

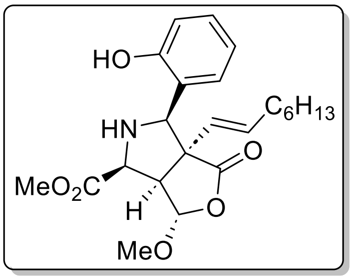
Methyl (3*S*,3a*R*,4*S*,6*S*,6a*R*)-6-(2-hydroxyphenyl)-3-methoxy-1-oxo-6a-(1-(triisopropylsilyl)-1*H*-pyrrol-3-yl)hexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (4x):



The reaction of methyl (*E*)-2-((2-hydroxybenzylidene)amino)acetate (**1b**) (19.3 mg, 0.1 mmol), 5-methoxy-3-(1-(triisopropylsilyl)-1*H*-pyrrol-3-yl)furan-2(5*H*)-one (**(±)-2f**) (33.5 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4x** as a white solid (25 mg, 47% yield) and **(–)-2f** as a brown oil (13.1 mg, 39% yield). The enantiomeric excess for **4x** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 4.29 min, τ_{major} = 4.60 min (97% *ee*). $[\alpha]^{20}_D$ = 0.116 (c = 0.45, $CHCl_3$). The enantiomeric excess for **(–)-2f** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm , τ_{minor} = 1.37 min, τ_{major} = 1.22 min (17% *ee*). $[\alpha]^{20}_D$ = – 0.019 (c = 0.39, $CHCl_3$). **c = 15%**, ***s* = 120** (Calculated as *s* = 117).

^{1}H NMR (300 MHz, $CDCl_3$) *δ:* 9.80 (brs, 1H), 7.25 – 7.14 (m, 1H), 6.85 (d, *J* = 8.2 Hz, 1H), 6.81 – 6.75 (m, 2H), 6.72 – 6.66 (m, 2H), 6.24 (d, *J* = 2.5 Hz, 1H), 5.25 (d, *J* = 2.9 Hz, 1H), 4.40 (s, 1H), 4.33 (d, *J* = 6.8 Hz, 1H), 3.87 (s, 3H), 3.48 (s, 3H), 3.42 (dd, *J* = 6.7, 3.0 Hz, 1H), 1.40 (sept, *J* = 7.9 Hz, 3H), 1.08 (d, *J* = 7.6, 9H), 1.07 (d, *J* = 7.6, 9H).**^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 173.5, 169.9, 157.7, 130.1, 129.5, 125.3, 123.0, 122.4, 119.1, 118.9, 117.4, 108.2, 104.6, 75.6, 62.0, 57.5, 57.2, 55.9, 52.7, 17.9, 11.7. **ESI-HRMS** calculated for $C_{28}H_{41}N_2O_6Si$ $(M+H)^+$: 529.2729; found: 529.2735.

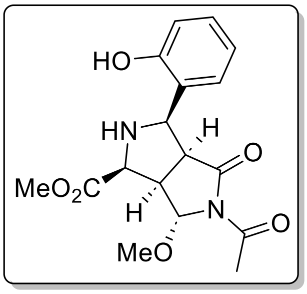
Methyl (3*S*,3a*R*,4*S*,6*S*,6a*S*)-6-(2-hydroxyphenyl)-3-methoxy-6a-((*E*)-oct-1-en-1-yl)-1-oxohexahydro-1*H*-furo[3,4-*c*]pyrrole-4-carboxylate (4y):



The reaction of methyl (*E*)-2-((2-hydroxybenzylidene)amino)acetate (**1b**) (19.3 mg, 0.1 mmol), (*E*)-5-methoxy-3-(oct-1-en-1-yl)furan-2(5*H*)-one (**(±)-2g**) (22.4 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4y** as a white solid (17 mg, 41% yield) and **(–)-2g** as a yellow oil (9.2 mg, 41% yield). The enantiomeric excess for **4y** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 4.11 min, τ_{major} = 4.53 min (93% *ee*). $[\alpha]^{20}_D$ = 0.081 (c = 0.49, $CHCl_3$). The enantiomeric excess for **(–)-2g** was determined by SFC on a *Daicel Chiralpak* IG column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm , τ_{minor} = 6.99 min, τ_{major} = 5.80 min (86% *ee*). $[\alpha]^{20}_D$ = – 0.141 (c = 0.32, $CHCl_3$). **c = 48%**, ***s* = 80** (Calculated as *s* = 79).

^{1}H NMR (300 MHz, $CDCl_3$) *δ:* 9.59 (brs, 1H), 7.22 (t, *J* = 7.7 Hz, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.83 (t, *J* = 8.2 Hz, 2H), 5.85 – 5.65 (m, 2H), 5.21 (d, *J* = 2.8 Hz, 1H), 4.25 (s, 1H), 4.14 (d, *J* = 6.9 Hz, 1H), 3.85 (s, 3H), 3.49 (s, 3H), 3.19 (dd, *J* = 6.3, 3.3 Hz, 1H), 2.09 (q, *J* = 6.9 Hz, 2H), 1.45 – 1.19 (m, 8H), 0.89 (t, *J* = 6.5 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 173.4, 169.7, 157.7, 133.3, 130.3, 129.1, 126.9, 119.6, 118.6, 117.7, 104.5, 74.3, 61.5, 59.2, 57.6, 53.4, 52.8, 32.7, 31.8, 29.1, 28.9, 22.7, 14.2. **ESI-HRMS** calculated for $C_{23}H_{32}NO_6$ $(M+H)^+$: 418.2225; found: 418.2231.

Methyl (1*S*,3*R*,3a*S*,6*R*,6a*R*)-5-acetyl-3-(2-hydroxyphenyl)-6-methoxy-4-oxooctahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (4z):

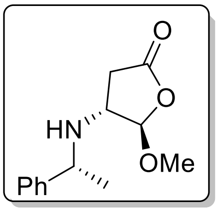


The reaction of methyl (*E*)-2-((2-hydroxybenzylidene)amino)acetate (**1b**) (19.3 mg, 0.1 mmol), 1-acetyl-5-methoxy-1*H*-pyrrol-2(5*H*)-one (**(±)-2h**) (15.5 mg, 0.1 mmol), and Takemoto's catalyst **3a** (8.2 mg, 20 mol%) in *p*-xylene (0.3 mL, [0.33]M) following the general procedure **GP3** and purification by flash column chromatography (Cy:EtOAc = 40:60), yielded de compound **4z** as a white solid (16.3 mg, 47% yield) and **(–)-2h** as a colorless oil (6 mg, 39% yield). The enantiomeric excess for **4z** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 4.56 min, τ_{major} = 5.18 min (7% *ee*). The enantiomeric excess for **(–)-2h** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm , τ_{minor} = 1.55 min, τ_{major} = 2.39 min (3% *ee*). **c = n.d.**, ***s* = n.d.**

^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 7.25 – 7.18 (m, 1H), 7.06 (d, *J* = 7.3 Hz, 1H), 6.89 – 6.78 (m, 2H), 5.26 (t, *J* = 1.2 Hz, 1H), 4.62 (d, *J* = 8.5 Hz, 1H), 4.17 (d, *J* = 8.4 Hz, 1H), 3.86 (s, 3H), 3.50 – 3.40 (m, 4H), 3.21 – 3.12 (m, 1H), 2.37 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) *δ*: 171.7, 171.2, 170.3, 157.9, 130.1, 128.9, 119.7, 119.5, 117.4, 88.8, 65.7, 62.2, 57.5, 52.9, 51.1, 44.5, 24.8. **ESI-HRMS** calculated for $C_{17}H_{21}N_2O_6$ $(M+H)^+$: 349.1395; found: 349.1401.

Further derivatizations of (–)-2a in one pot and direct procedures.

(4*R*,5*R*)-5-methoxy-4-(((*R*)-1-phenylethyl)amino)dihydrofuran-2(3*H*)-one (**5**)**:**[12]



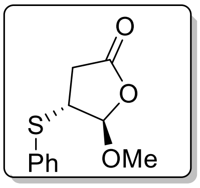
Procedure A: After Kinetic Resolution of (**(±)-2a**) by reaction with imine **1b**, (*S*)-1-phenylethanamine (12.1 mg, 0.1 mmol) was added *in-situ* to the reaction mixture and further stirred for another 24 h. The reaction was monitored by TLC. After completion, the solvent was evaporated under vacuum and purified by preparative TLC (Cy:EtOAc = 85:15) to yield the compound **5** as a yellow solid (10.6 mg, 45% yield). The enantiomeric excess for **5** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 3.35 min, τ_{major} = 3.15 min (88% *ee*). $[\alpha]^{20}_D$ = -0.058 (c = 0.1, $CHCl_3$).

Procedure B: To a solution of 5-methoxyfuran-2(5*H*)-one (**(–)-2a**) (5.7 mg, 0.05 mmol, 88% *ee*), obtained by kinetic resolution process, in *p*-xylene (0.15 mL, [0.33]M), (*S*)-1-phenylethanamine (12.1 mg, 0.1 mmol) was added. The reaction mixture was stirred at room temperature for 24 h. After completion, the solvent was evaporated under vacuum and purified by preparative TLC (Cy:EtOAc = 85:15) to yield the compound **5** as a yellow solid (10.4 mg, 88% yield). The enantiomeric excess for **5** was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 3.35 min, τ_{major} = 3.15 min (87% *ee*).

Spectroscopic data are in agreement with published data.[12]

^{1}H NMR (300 MHz, $CDCl_3$) *δ* (ppm): 7.39 – 7.28 (m, 5H), 4.90 (s, 1H), 3.81 (q, *J* = 6.6 Hz, 1H), 3.56 (s, 1H), 3.32 (s, 3H), 3.30 – 3.24 (m, 1H), 2.77 (dd, *J* = 17.7, 7.2 Hz, 1H), 2.39 – 2.29 (m, 1H), 1.38 (d, *J* = 6.6 Hz, 3H). **ESI-HRMS** calculated for $C_{13}H_{18}NO_3$ $(M+H)^+$: 236,1281; found: 236.1265.

(4*R*,5*R*)-5-methoxy-4-(phenylthio)dihydrofuran-2(3*H*)-one (6):[12]



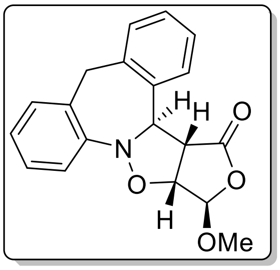
Procedure A: After Kinetic Resolution of (**(±)-2a**) by reaction with imine **1b**, *p*-xylene was evaporated under vacuum, and toluene (0.3 mL, [0.33]M) was added, and the reaction mixture was stirred for 5 min at −25 °C. At that time, benzenethiol (5.51 mg, 0.05 mmol) was added and the reaction was further stirred for another 24 h. The reaction was monitored by TLC. After completion, the solvent was evaporated under vacuum and purified by flash column chromatography on Iatrobeads silica gel (Cy:EtOAc = 95:5) to yield compound **6** as a yellow solid (9 mg, 44% yield). The enantiomeric excess for **6** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 2.49 min, τ_{major} = 2.64 min (91% *ee*). $[\alpha]^{20}_D$ = -0.029 (c = 0.2, $CHCl_3$).

Procedure B: To a solution of 5-methoxyfuran-2(5*H*)-one (**(–)-2a**) (5.7 mg, 0.05 mmol, 88% *ee*), obtained by kinetic resolution process, in toluene (0.15 mL, [0.33]M), benzenethiol (11 mg, 0.1 mmol) was added. The reaction mixture was stirred at -25 ºC for 24 h. After completion, the solvent was evaporated under vacuum and purified by flash column chromatography on Iatrobeads silica gel (Cy:EtOAc = 95:5) to yield compound **6** as a yellow solid (9 mg, 80% yield). The enantiomeric excess for **6** was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH (95:5), flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 2.49 min, τ_{major} = 2.64 min (90% *ee*).

Spectroscopic data are in agreement with published data.[13]

^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 7.47 – 7.30 (m, 5H), 5.26 (d, *J* = 1.3 Hz, 1H), 3.81 (ddd, *J* = 8.4, 3.0, 1.3 Hz, 1H), 3.45 (s, 3H), 3.09 (dd, *J* = 18.3, 8.3 Hz, 1H), 2.46 (dd, *J* = 18.4, 2.9 Hz, 1H). **^{13}C NMR** (76 MHz, $CDCl_3$) *δ*: δ 174.3, 132.3, 131.9, 129.6, 128.3, 108.5, 57.1, 46.5, 33.9. **ESI-HRMS** calculated for $C_{11}H_{13}O_3S$ $(M+H)^+$: 225,0580; found: 225.0572.

(1*R*,3a*S*,3b*R*,14a*R*)-1-methoxy-3a,3b,8,14a-tetrahydrodibenzo[*c*,*f*]furo[3',4':4,5]isoxazolo[2,3-*a*]azepin-3(1*H*)-one (7):[14]



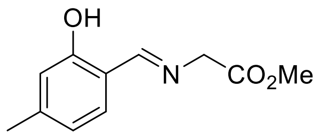
Procedure A: After Kinetic Resolution of (**(±)-2a**) by reaction with imine **1b**, 11*H*-dibenzo[*b*,*e*]azepine 5-oxide (10.5 mg, 0.05 mmol) was added *in-situ* to the reaction mixture and further stirred for another 2 h. The reaction was monitored by TLC. After completion, the solvent was evaporated under vacuum and purified by flash column chromatography on Iatrobeads silica gel (Cy:EtOAc = 90:10) to yield the compound **7** as a white solid (14.8 mg, 46% yield). The enantiomeric excess for **7** was determined by SFC on a *Daicel Chiralpak* IC column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 4.60 min, τ_{major} = 4.34 min (91% *ee*). $[\alpha]^{20}_{D}$ = -0.07 (c = 0.16, $CHCl_3$).

Procedure B: To a solution of 5-methoxyfuran-2(5*H*)-one (**(–)-2a**) (5.7 mg, 0.05 mmol, 88% *ee*), obtained by kinetic resolution process, in *p*-xylene (0.15 mL, [0.33]M), 11*H*-dibenzo[*b*,*e*]azepine 5-oxide (21 mg, 0.1 mmol) was added. The reaction mixture was stirred at room temperature for 2 h. After completion, the solvent was evaporated under vacuum and purified by flash column chromatography on Iatrobeads silica gel (Cy:EtOAc = 90:10) to yield the compound **7** as a white solid (15.1 mg, 93% yield). The enantiomeric excess for **7** was determined by SFC on a *Daicel Chiralpak* IC column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 4.60 min, τ_{major} = 4.34 min (90% *ee*).

Spectroscopic data are in agreement with published data.[14]

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.63 (d, *J* = 7.3 Hz, 1H), 7.35 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.25 – 7.18 (m, 5H), 7.04 (td, *J* = 7.4, 1.3 Hz, 1H), 5.60 (s, 1H), 4.83 (d, *J* = 6.8 Hz, 1H), 4.65 (d, *J* = 5.7 Hz, 1H), 4.42 (d, *J* = 14.7 Hz, 1H), 3.96 (dd, *J* = 6.7, 5.7 Hz, 1H), 3.82 (d, *J* = 14.7 Hz, 1H), 3.62 (s, 3H). **ESI-HRMS** calculated for $C_{19}H_{18}NO_4$ $(M+H)^+$: 324,1230; found: 324.1248.

NMR Spectra



1c

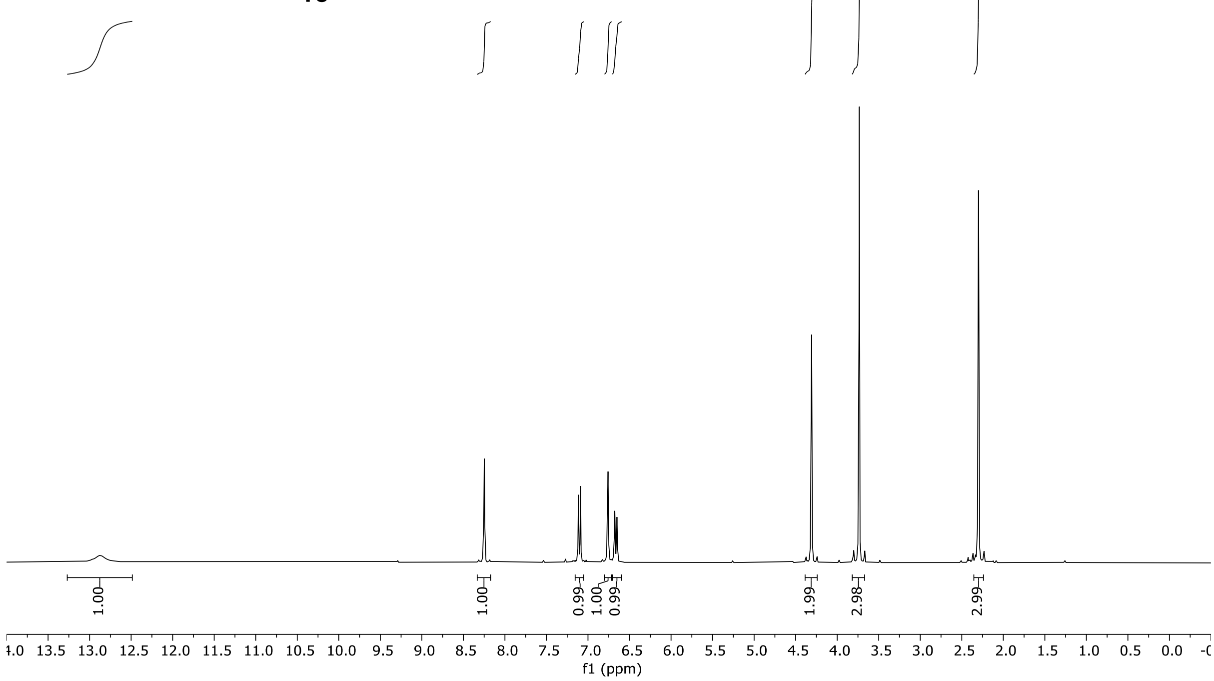


Figure S1. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **1c**.

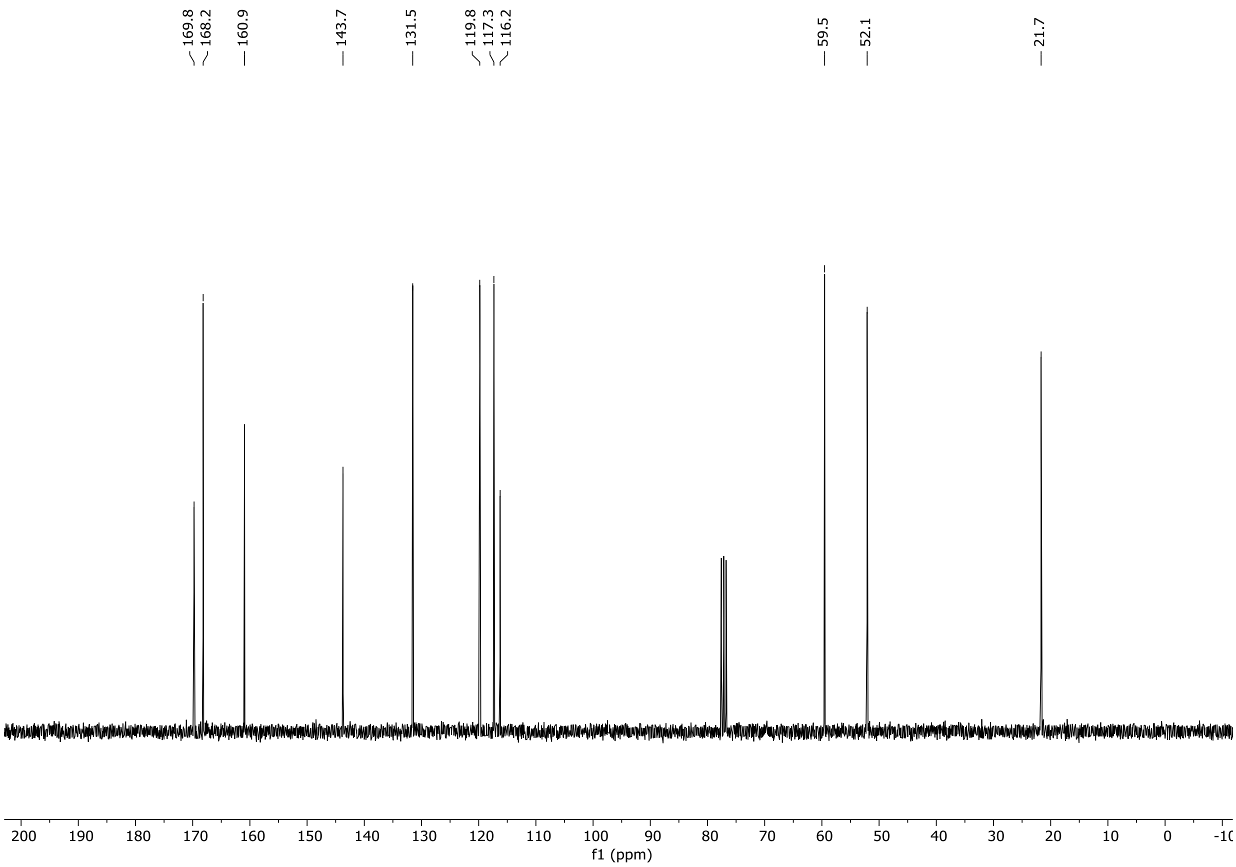


Figure S2. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **1c**.

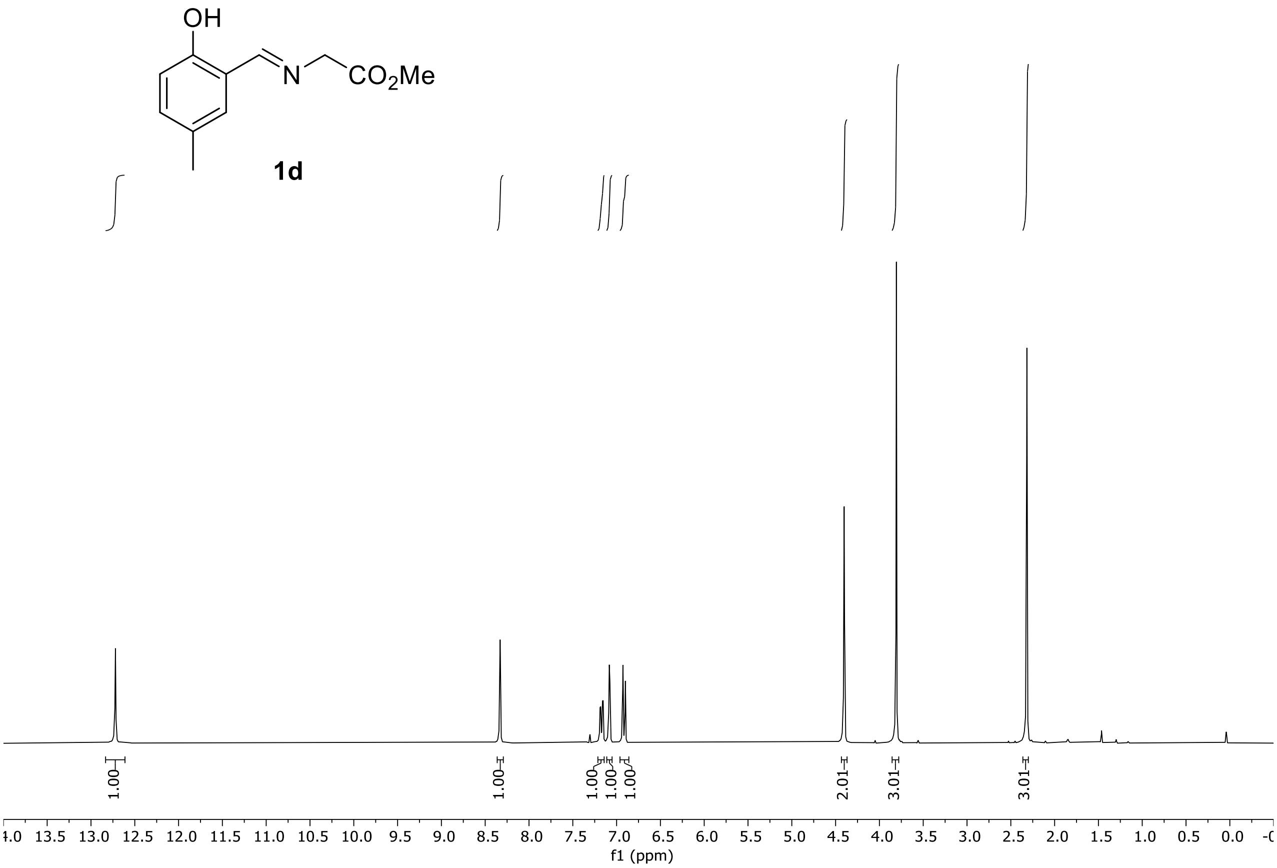


Figure S3. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **1d**.

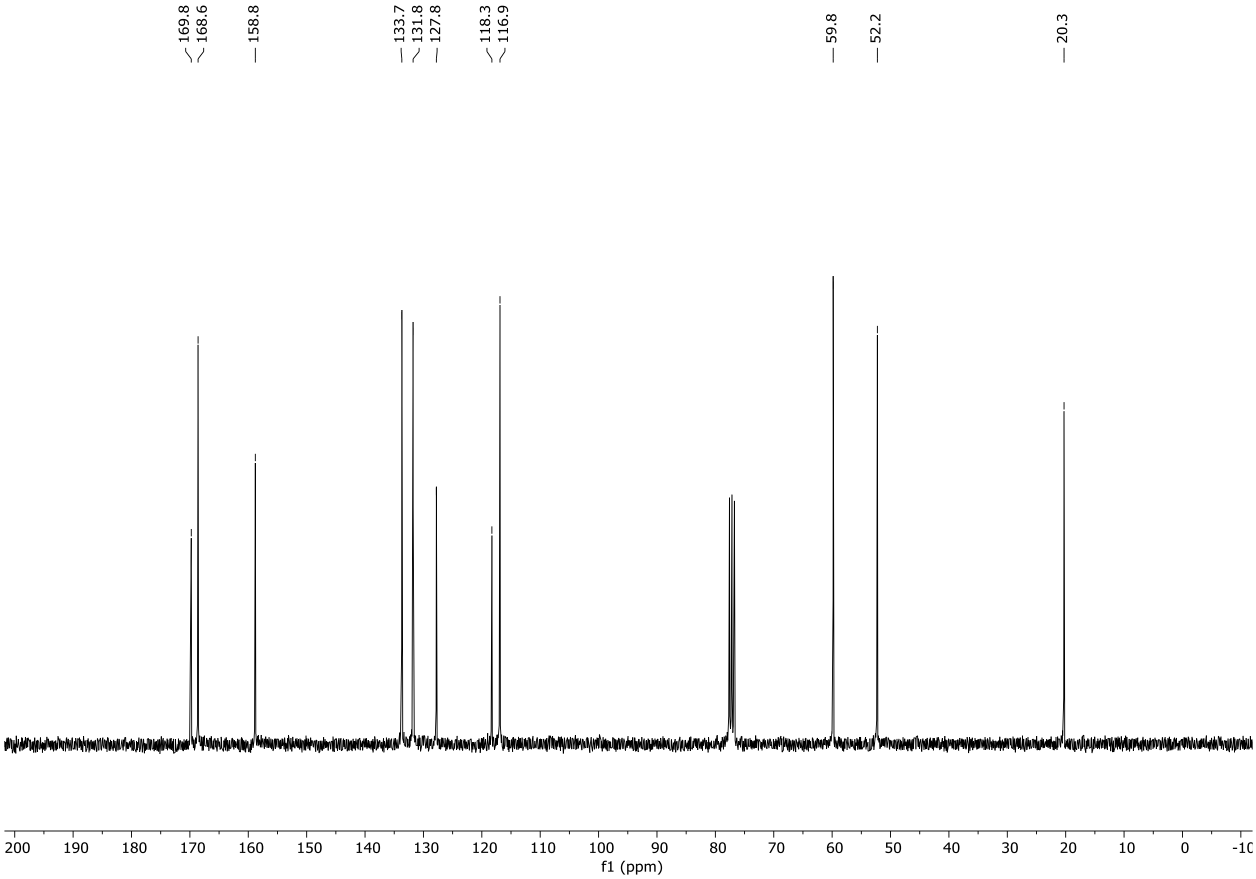


Figure S4. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **1d**.

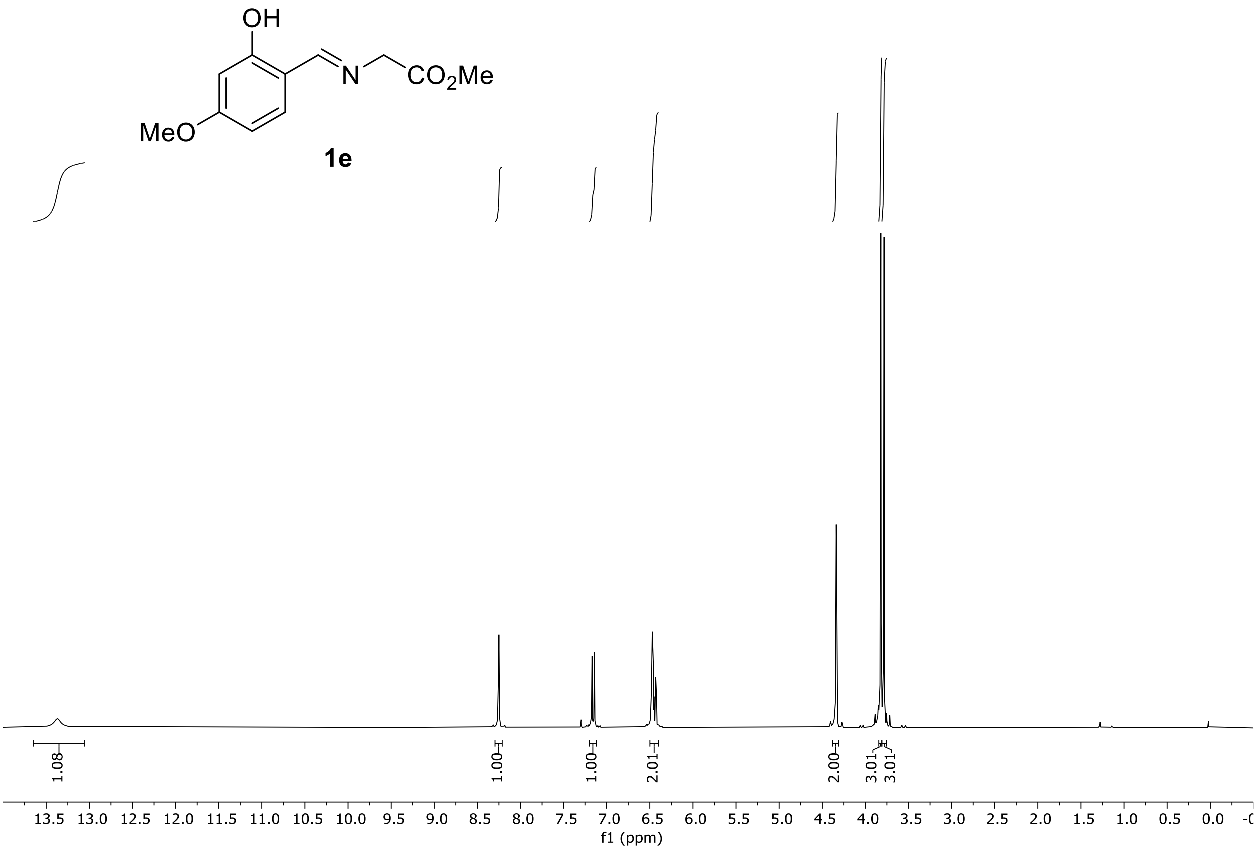


Figure S5. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **1e**.

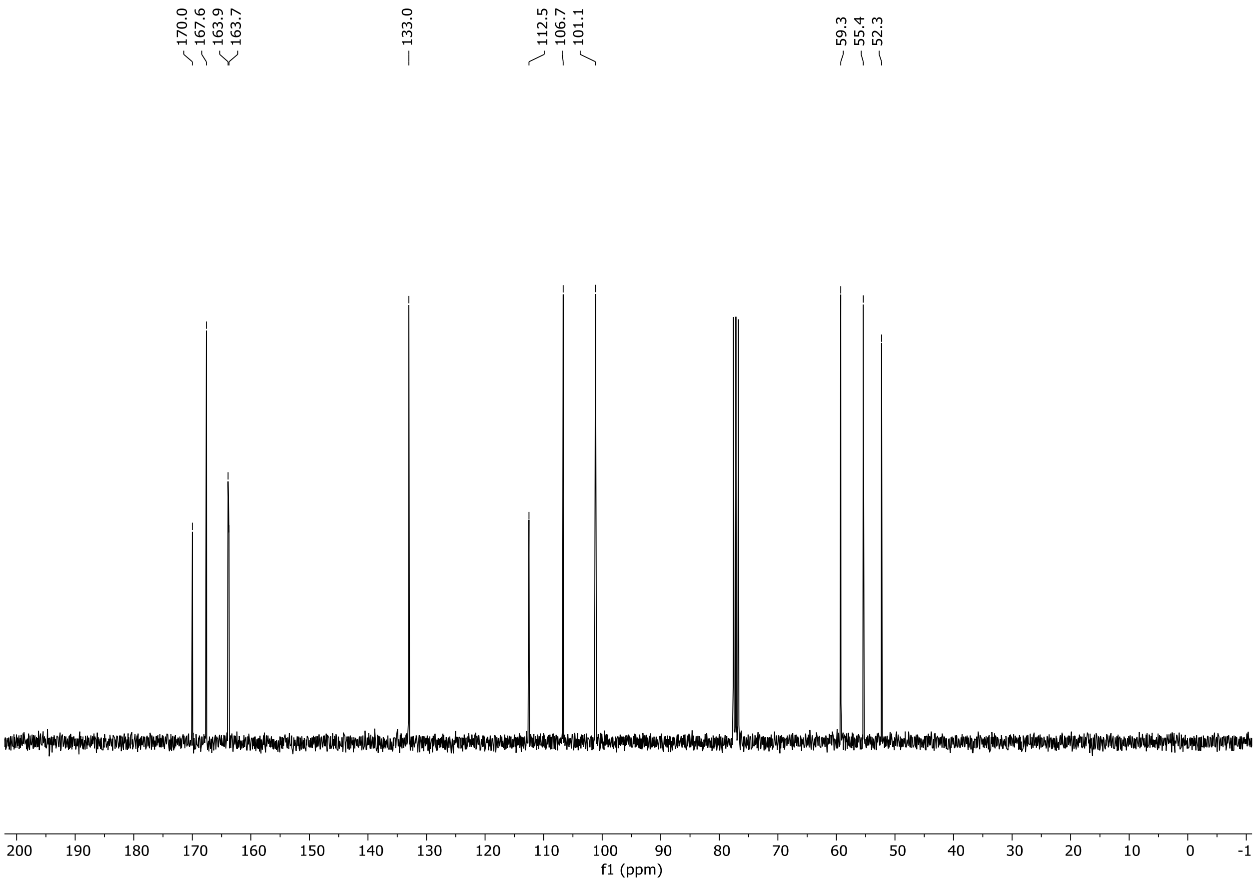
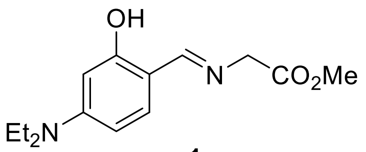


Figure S6. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **1e**.



1g

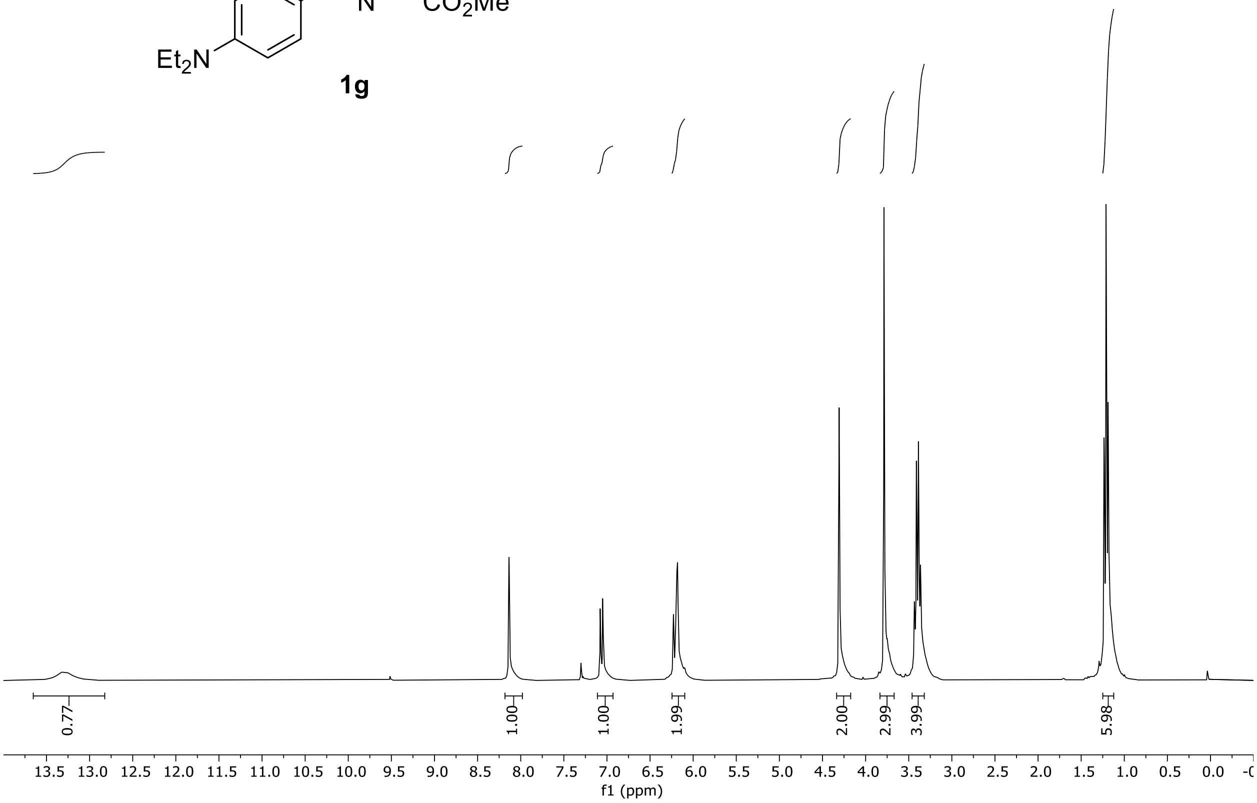


Figure S7. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **1g**.

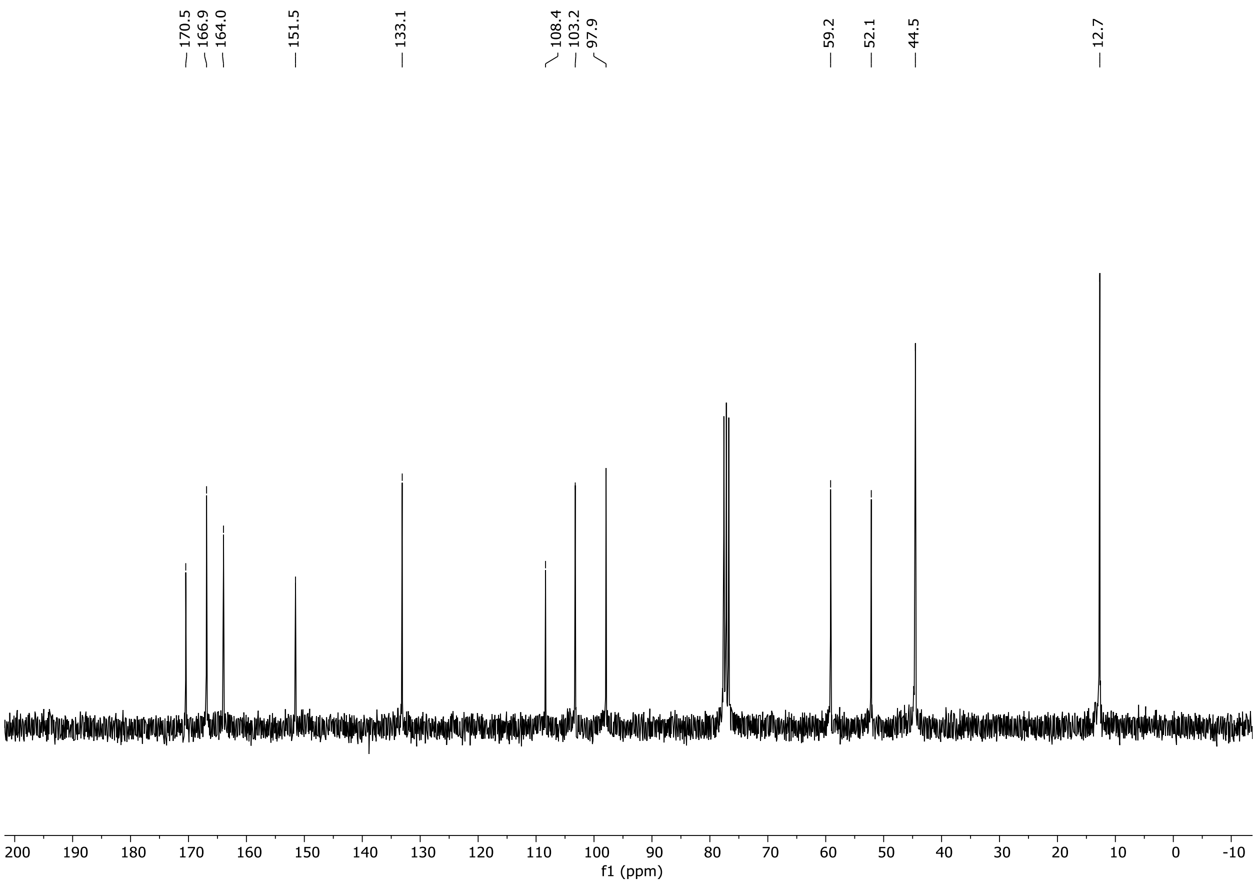
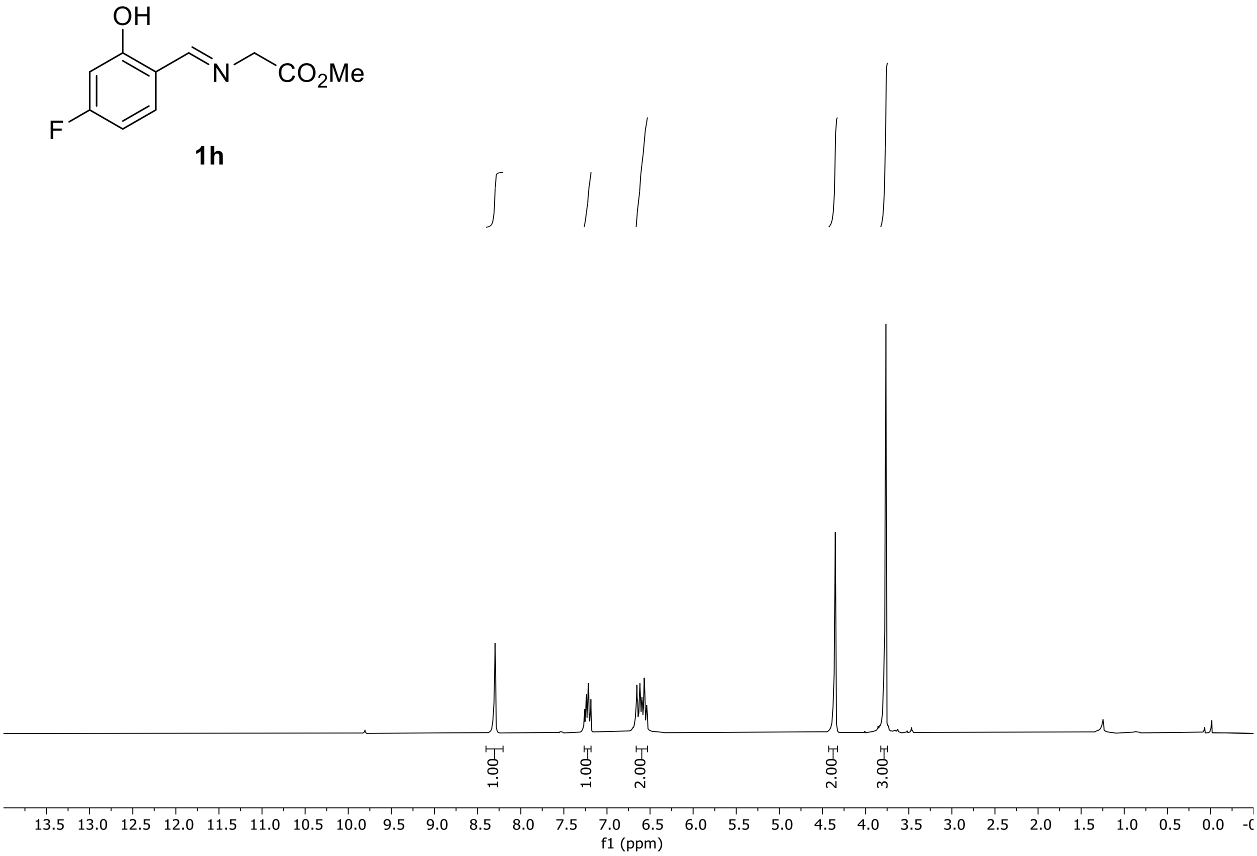


Figure S8. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **1g**.



1h

Figure S9. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **1h**.

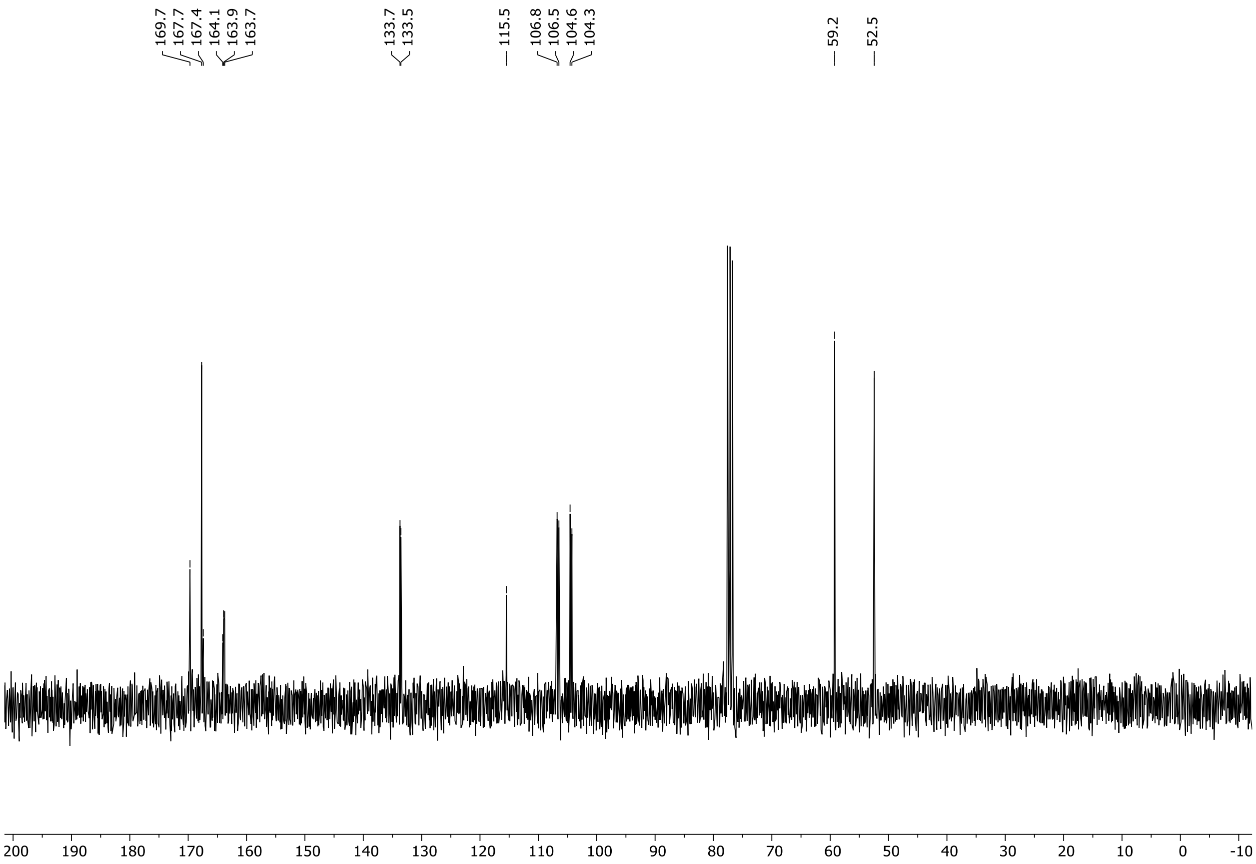
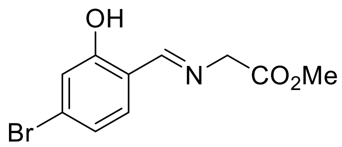


Figure S10. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **1h**.



1i

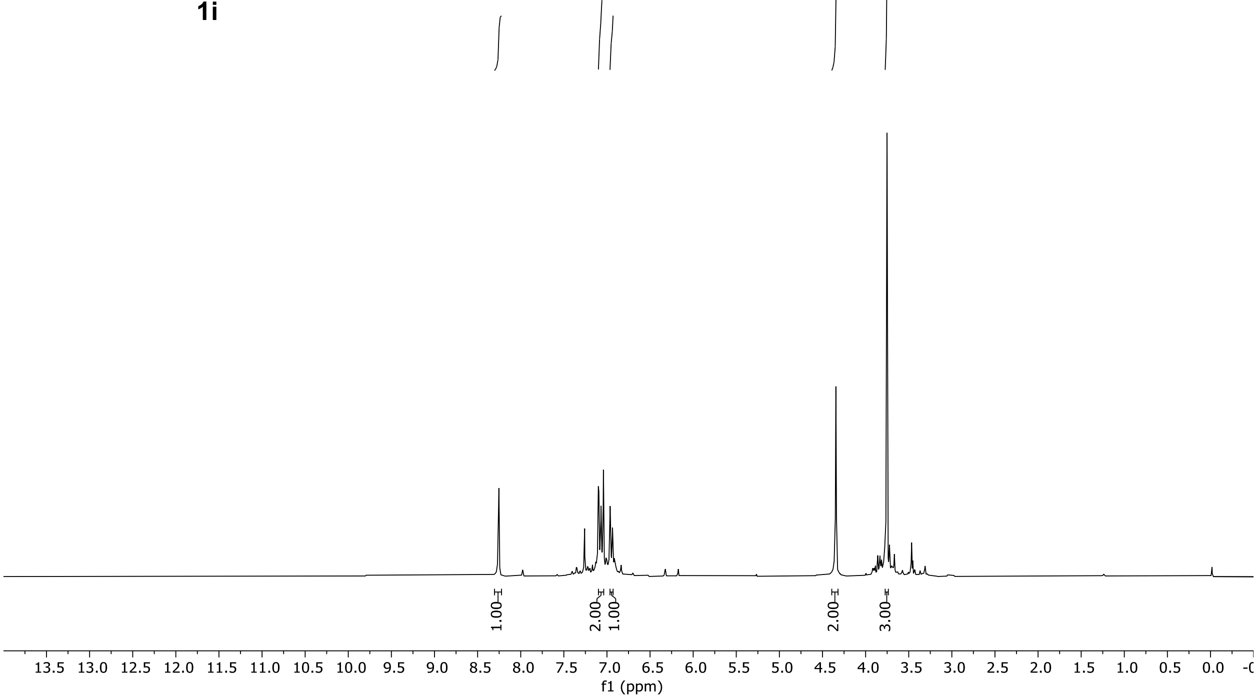


Figure S11. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **1i**.

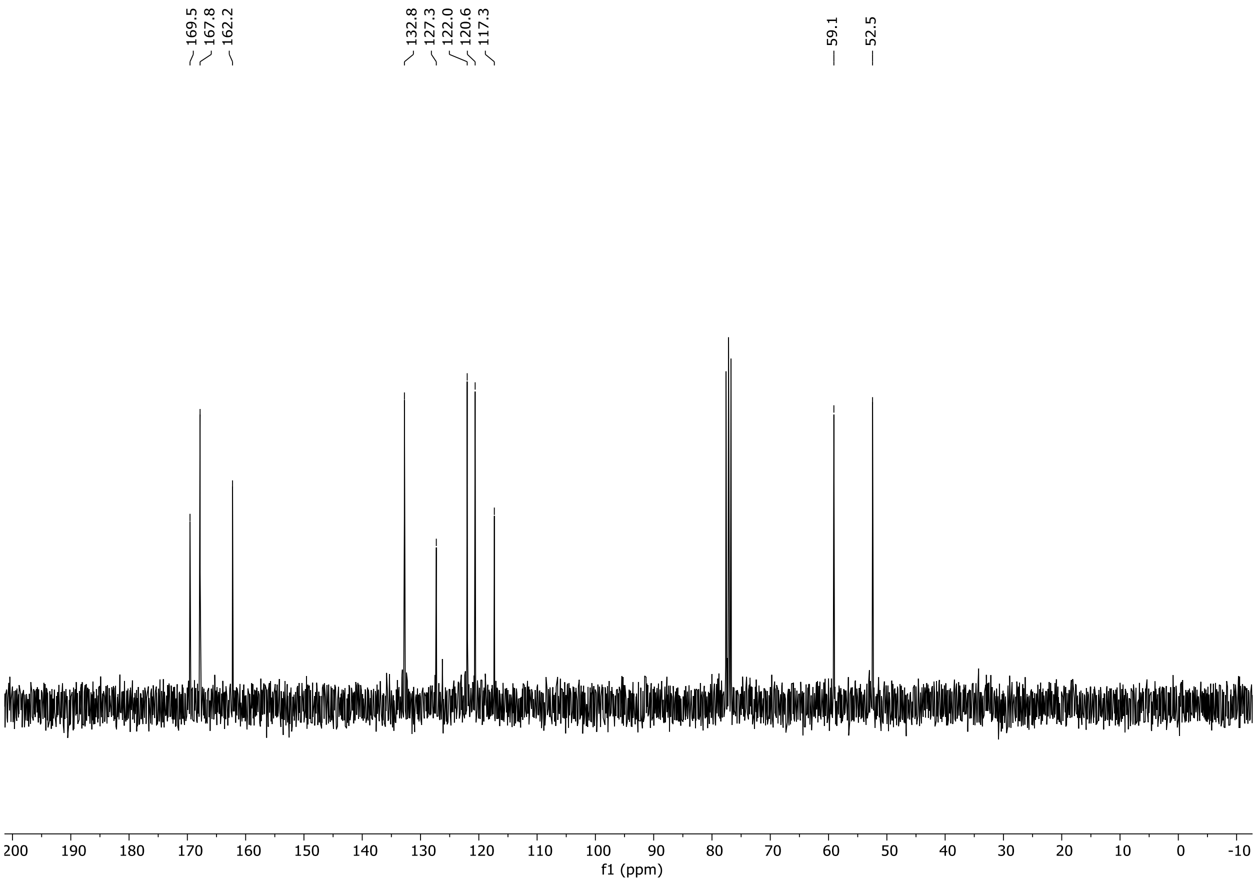


Figure S12. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **1i**.

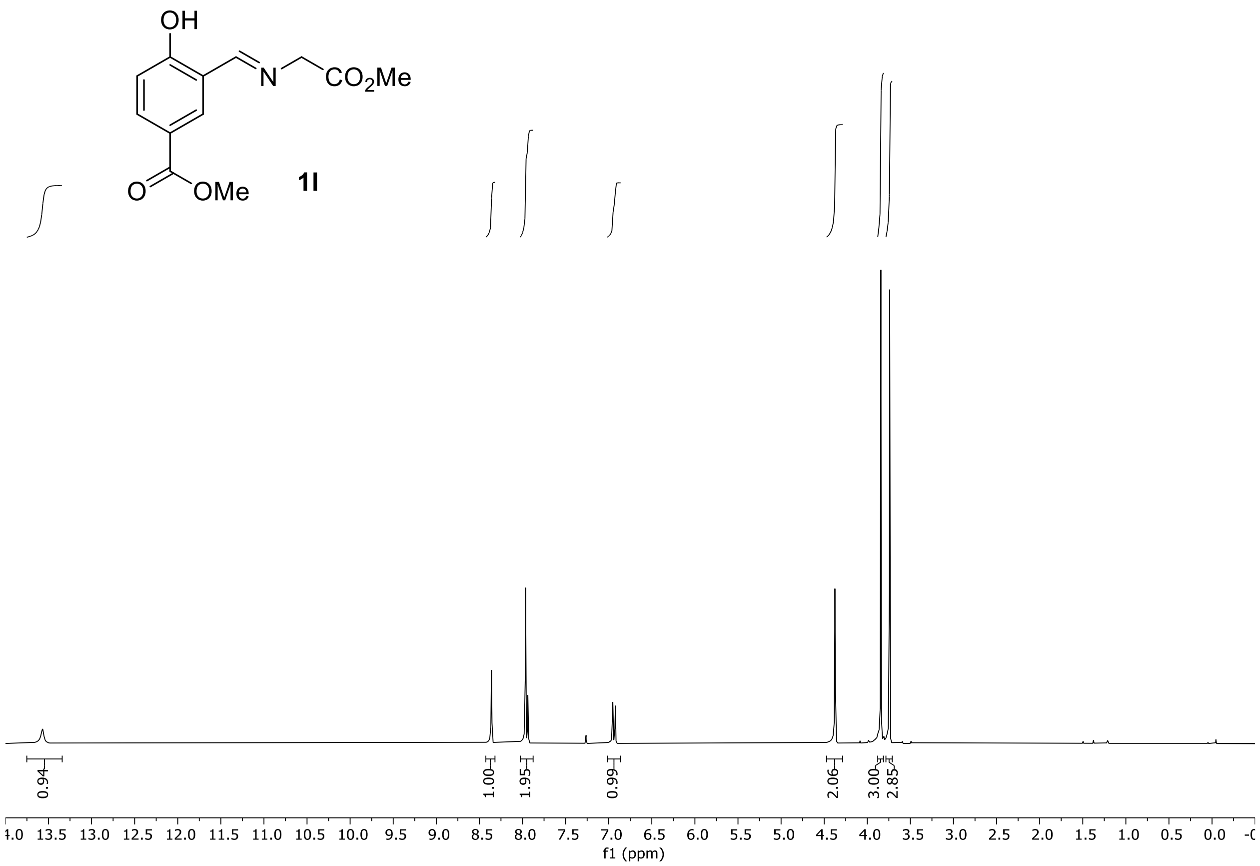


Figure S13. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **1l**.

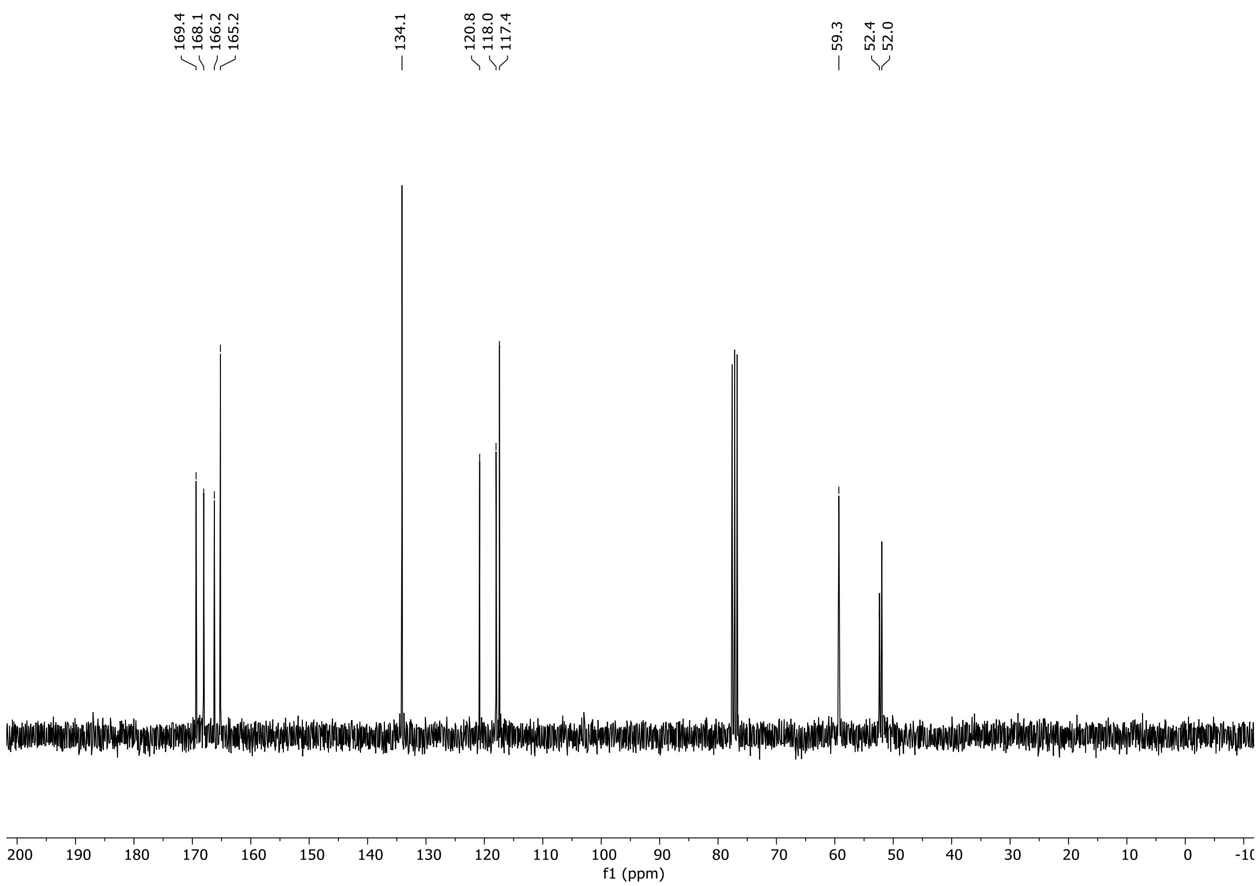
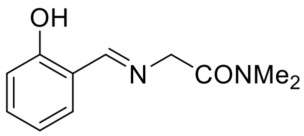


Figure S14. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **1l**.



1q

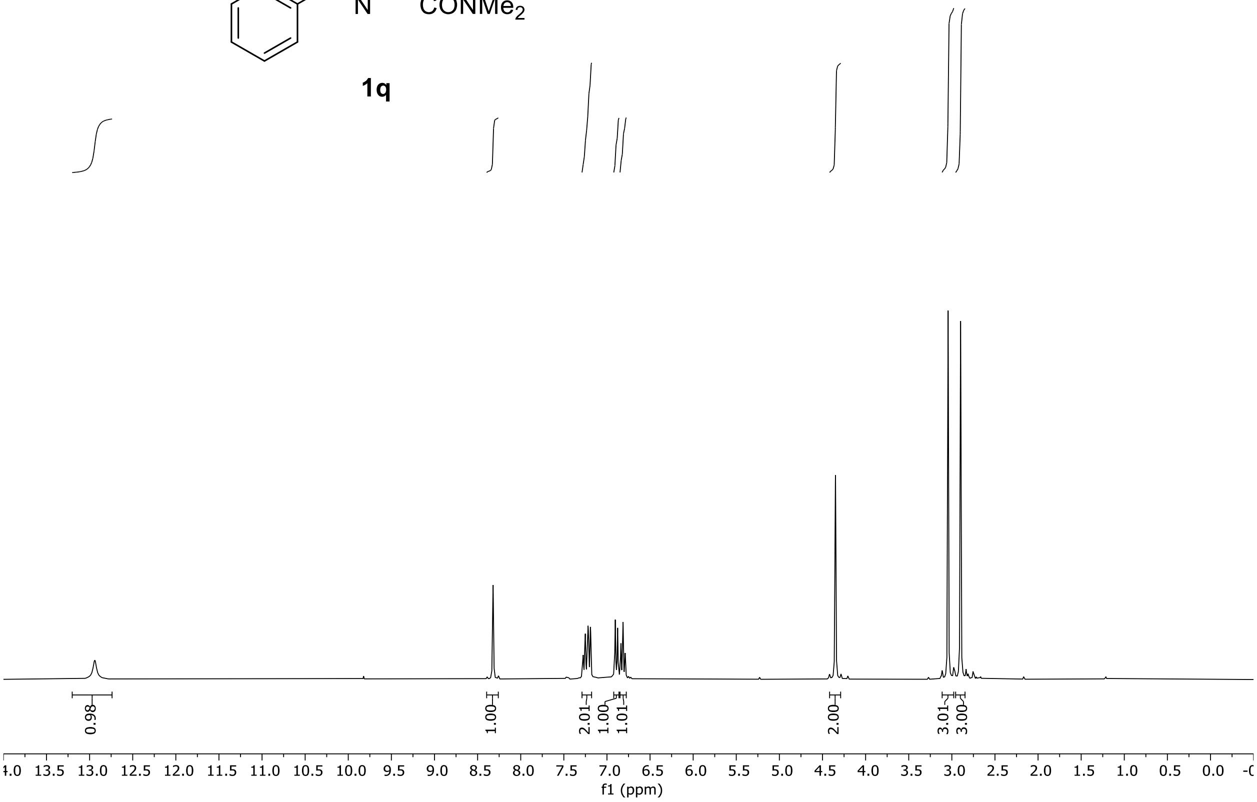


Figure S15. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **1q**.

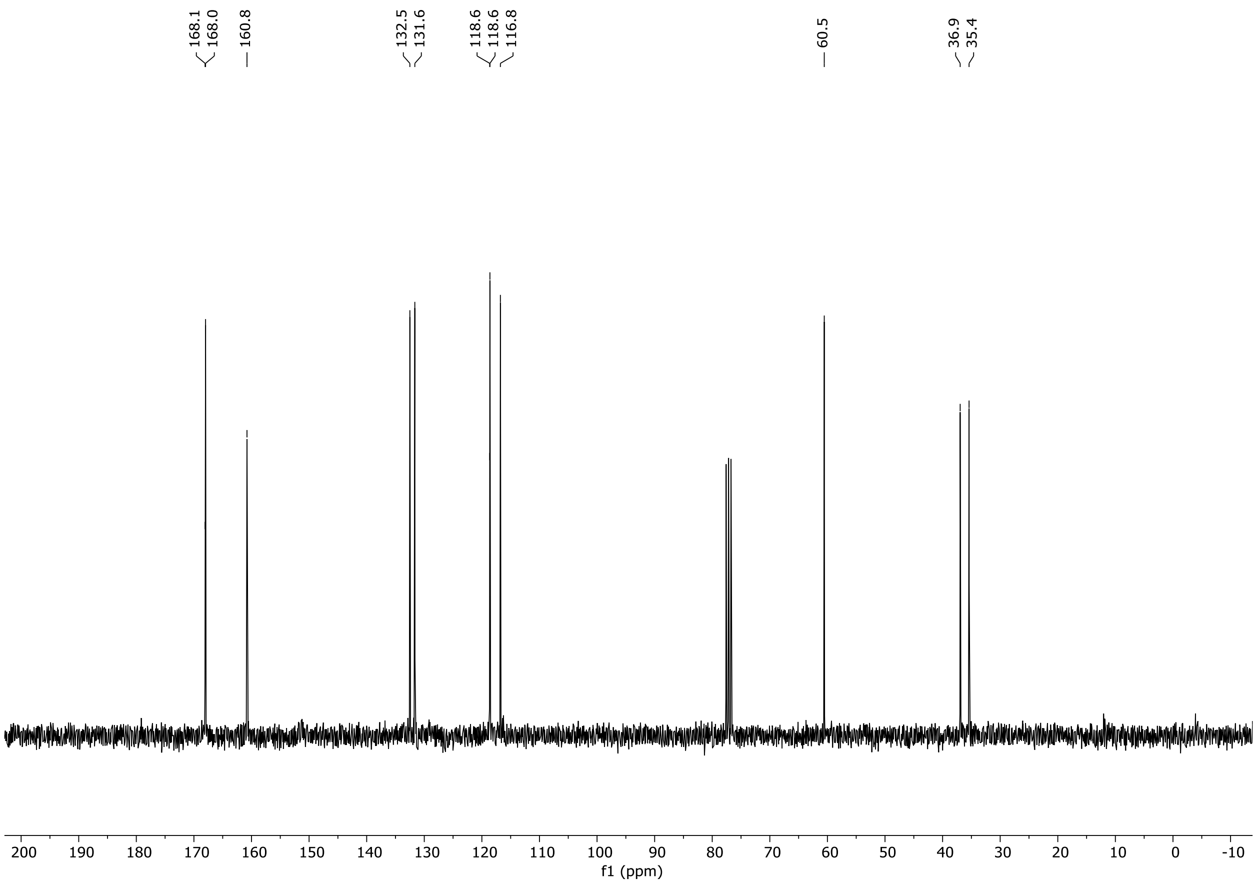


Figure S16. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **1q**.

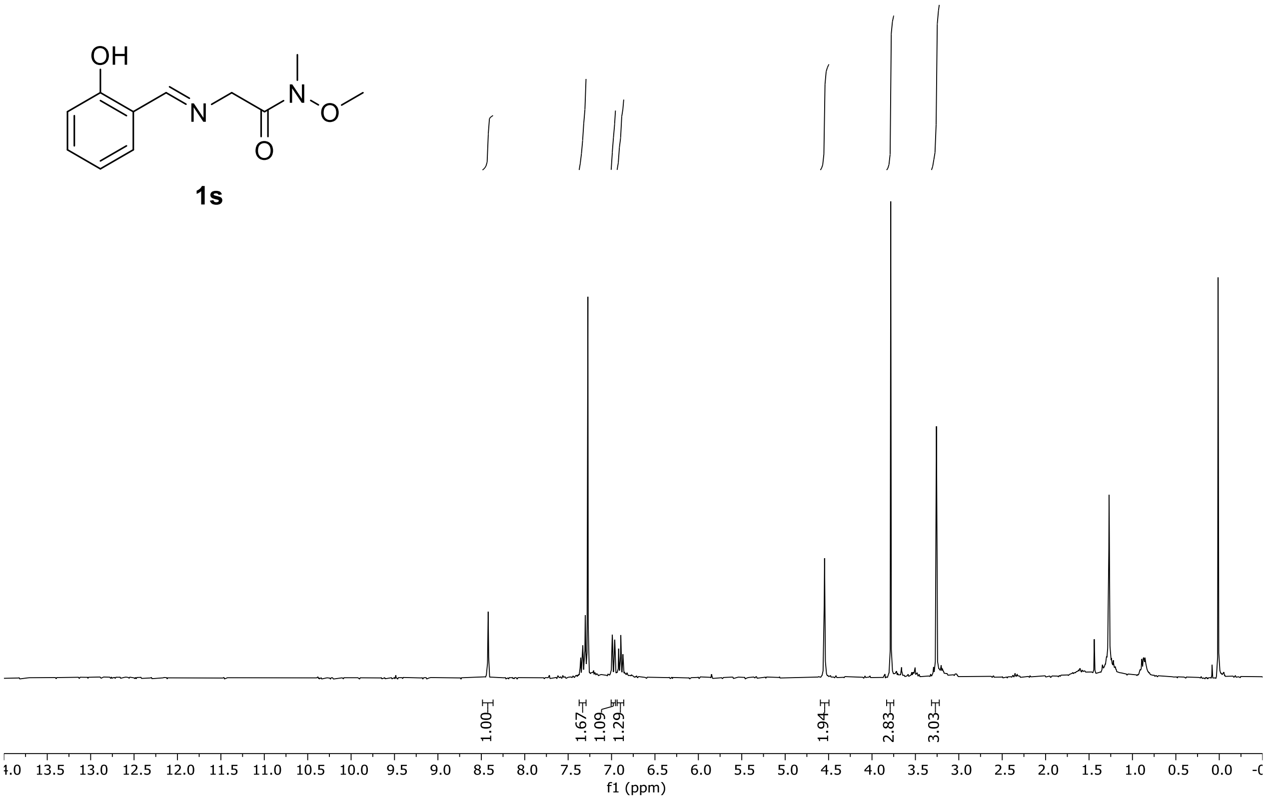


Figure S17. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **1s**.

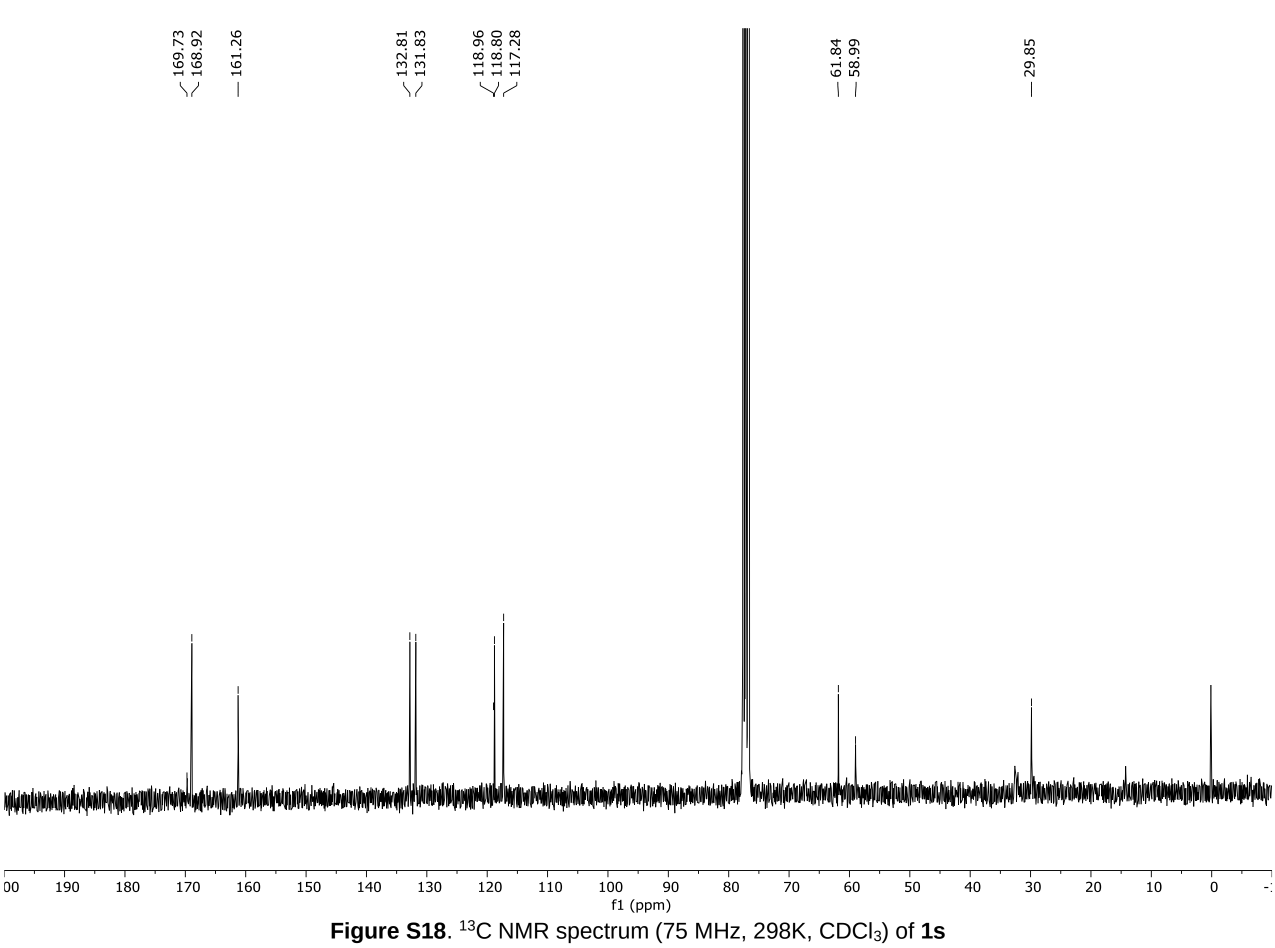


Figure S18. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **1s**

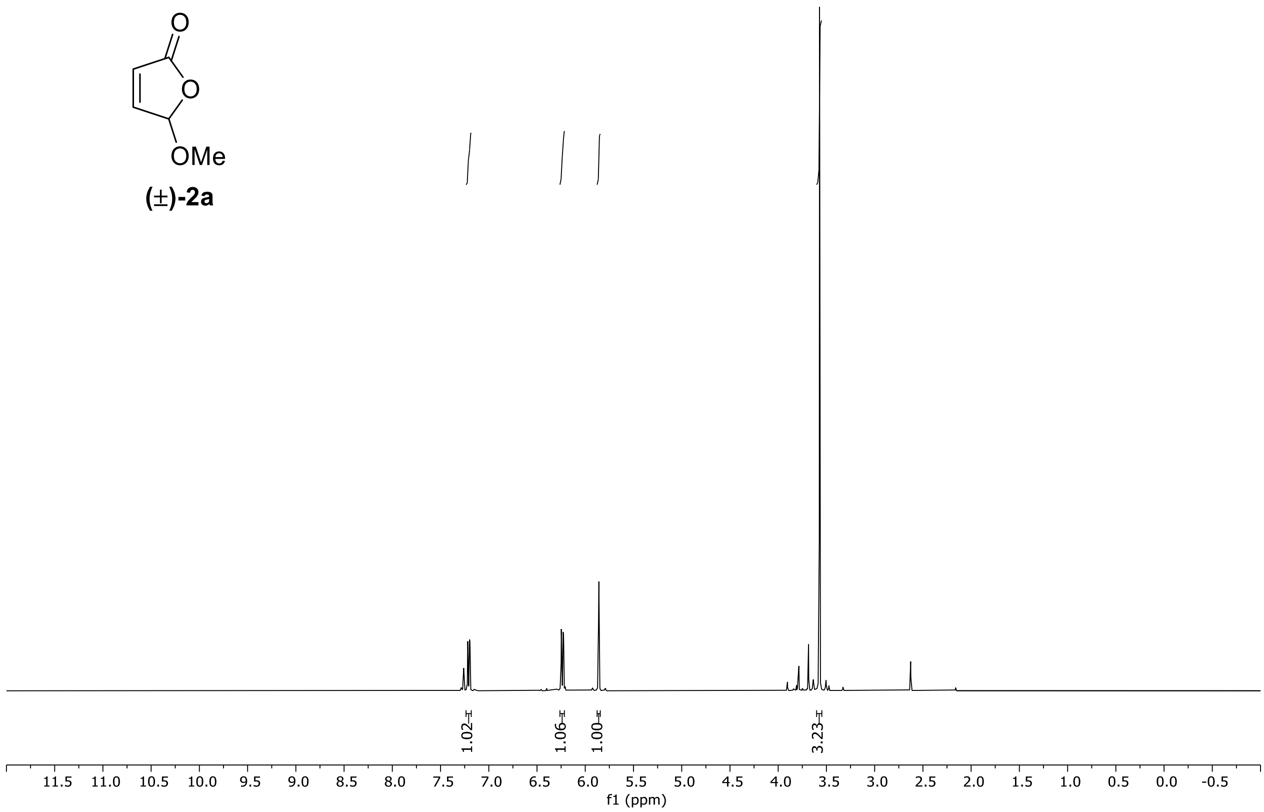


Figure S19. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **(±)-2a**.

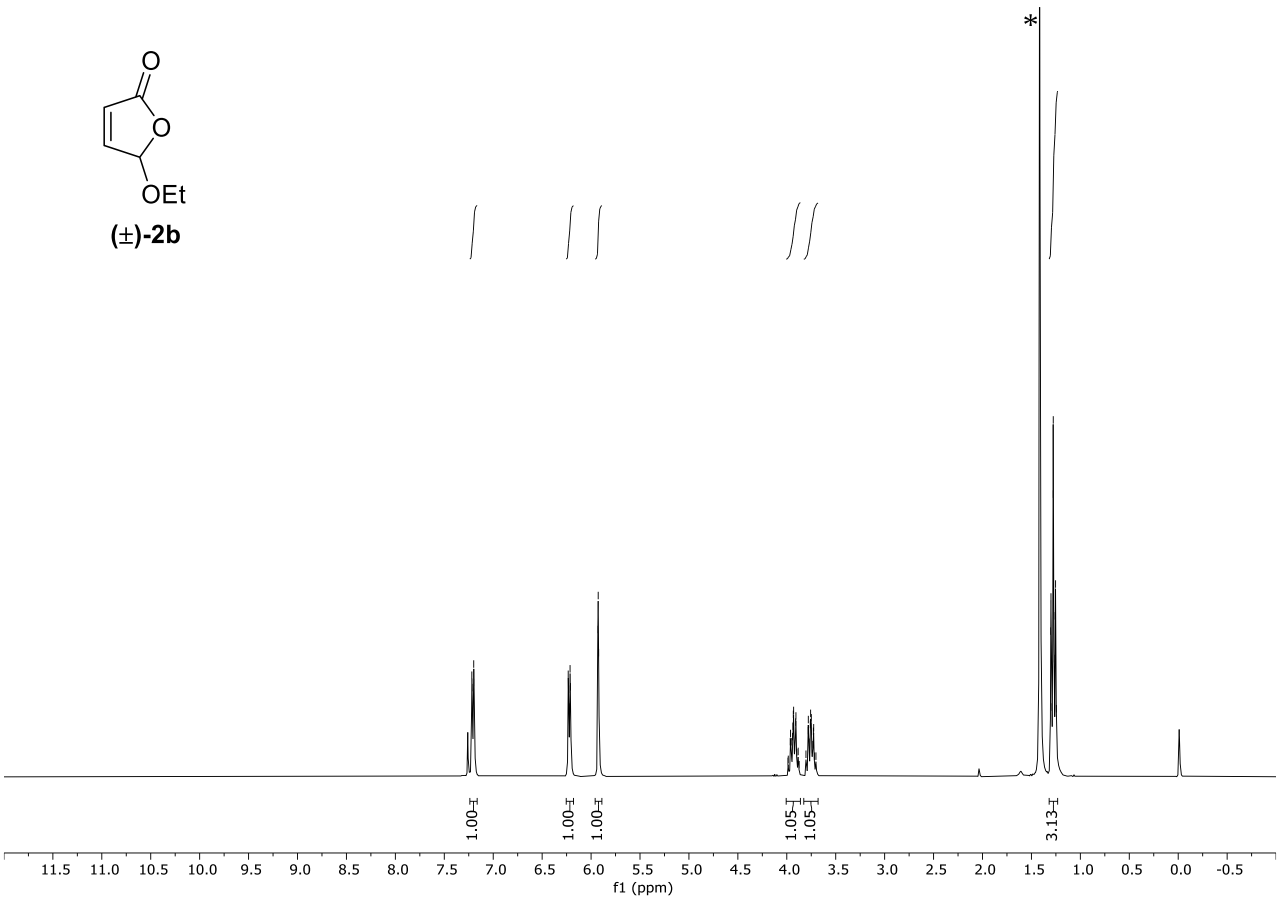


Figure S20. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **(±)-2b** (*Cyclohexane solvent peak).

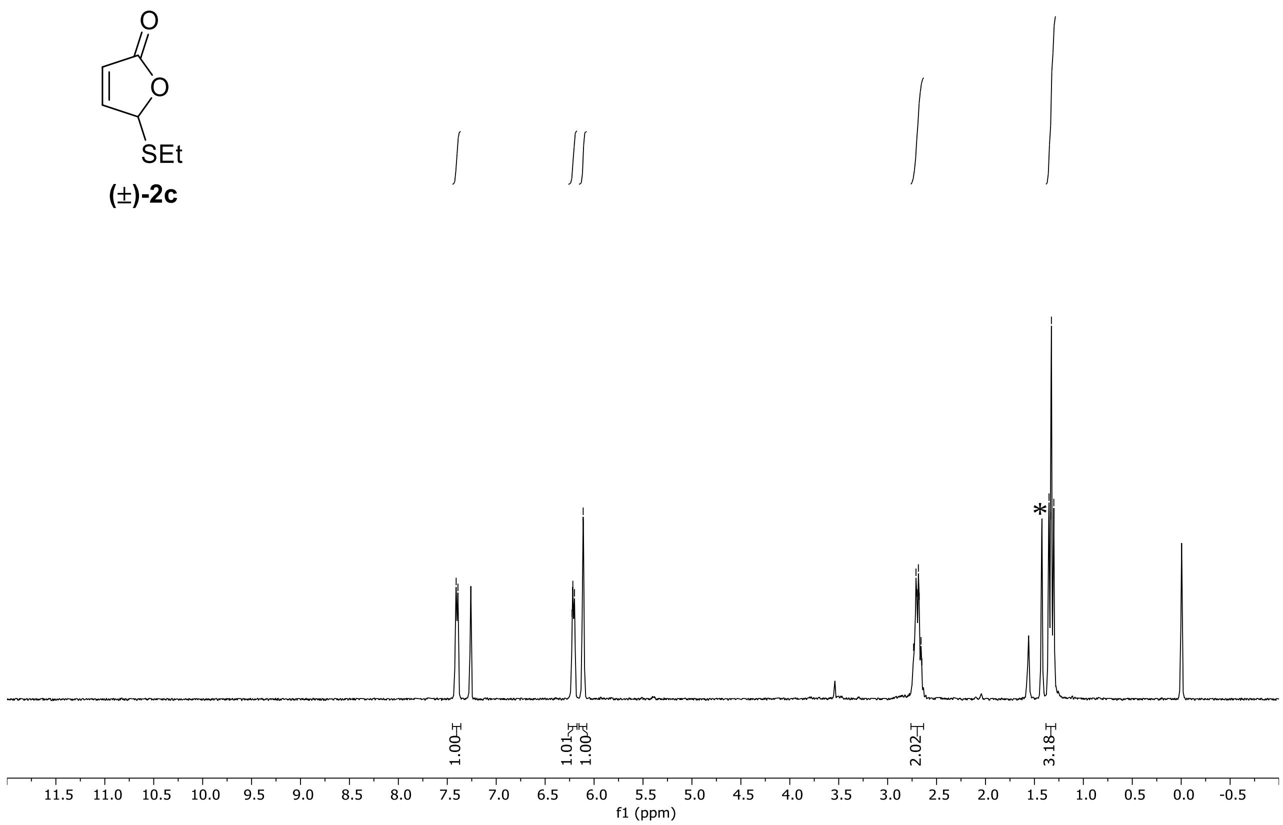


Figure S21. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **(±)-2c** (*Cyclohexane solvent peak).

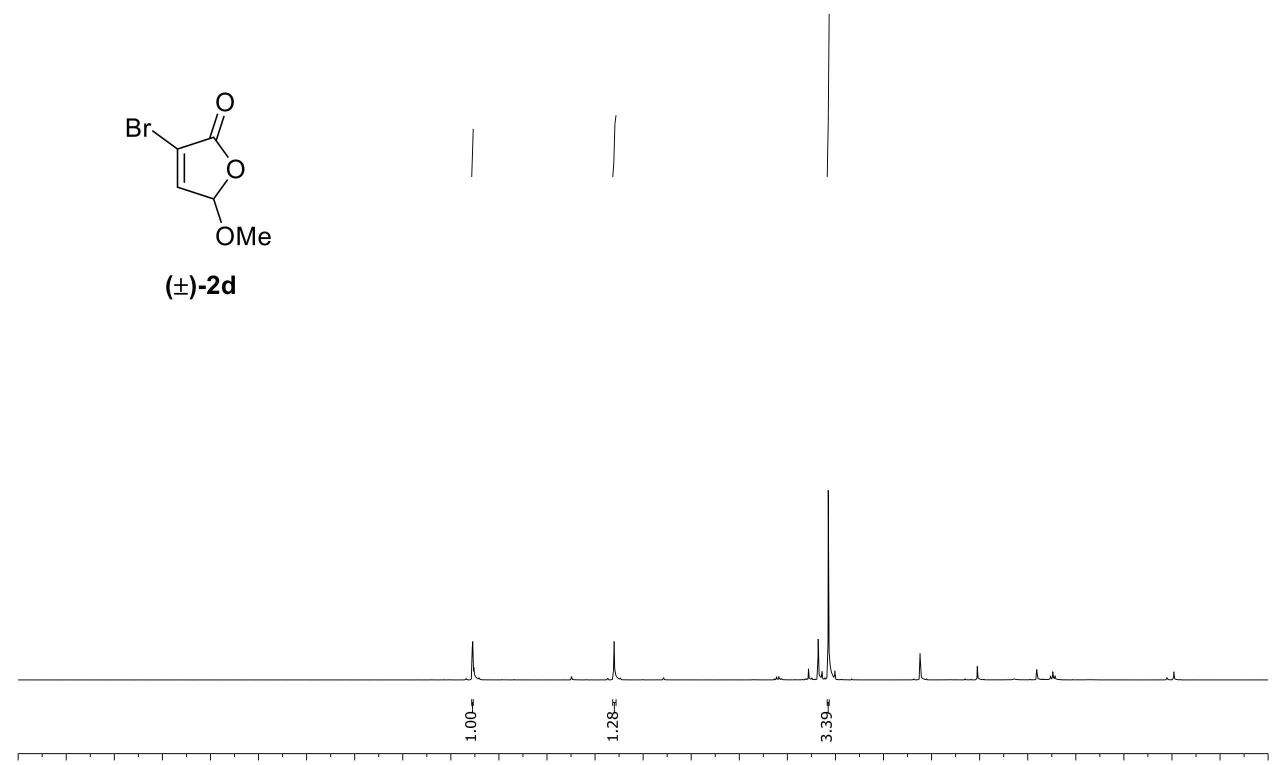


Figure S22. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **(±)-2d**.

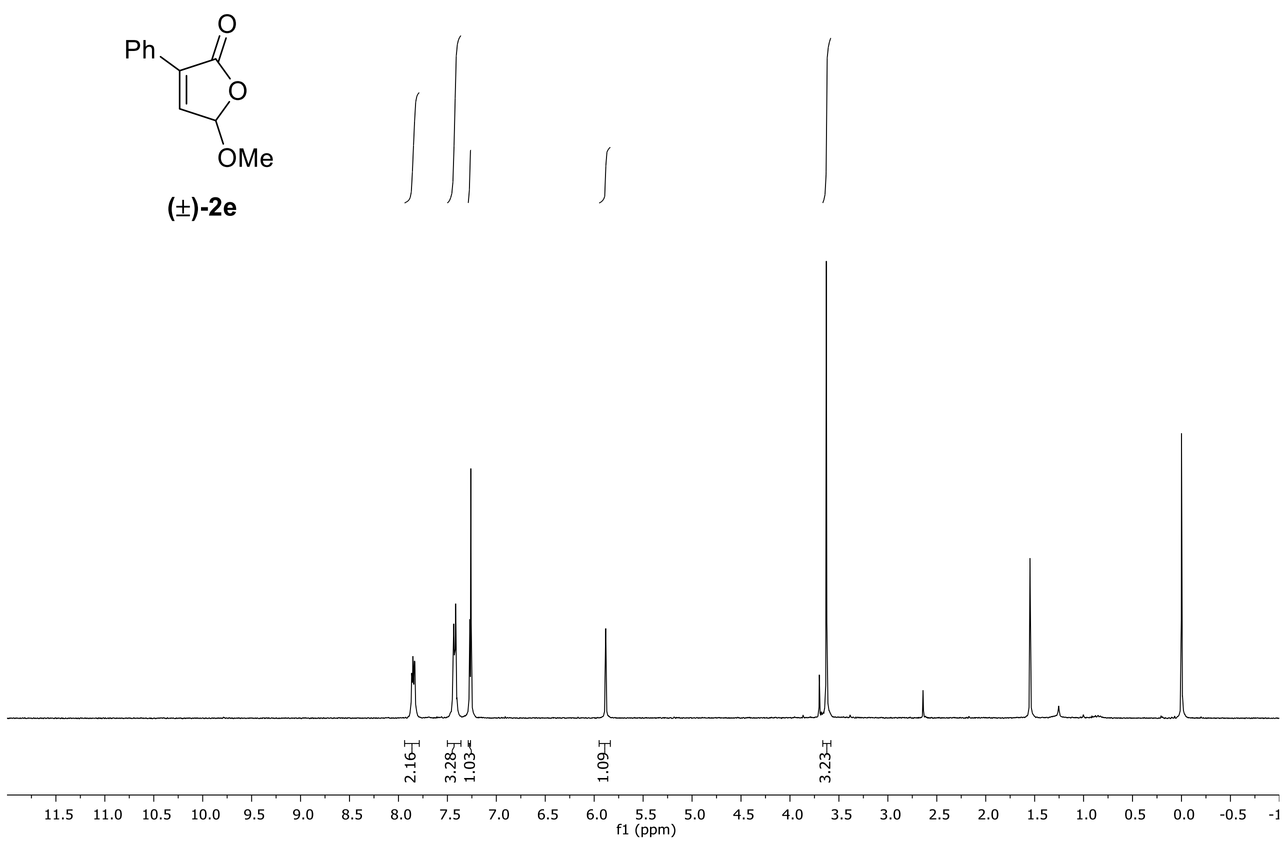


Figure S23. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **(±)-2e**.

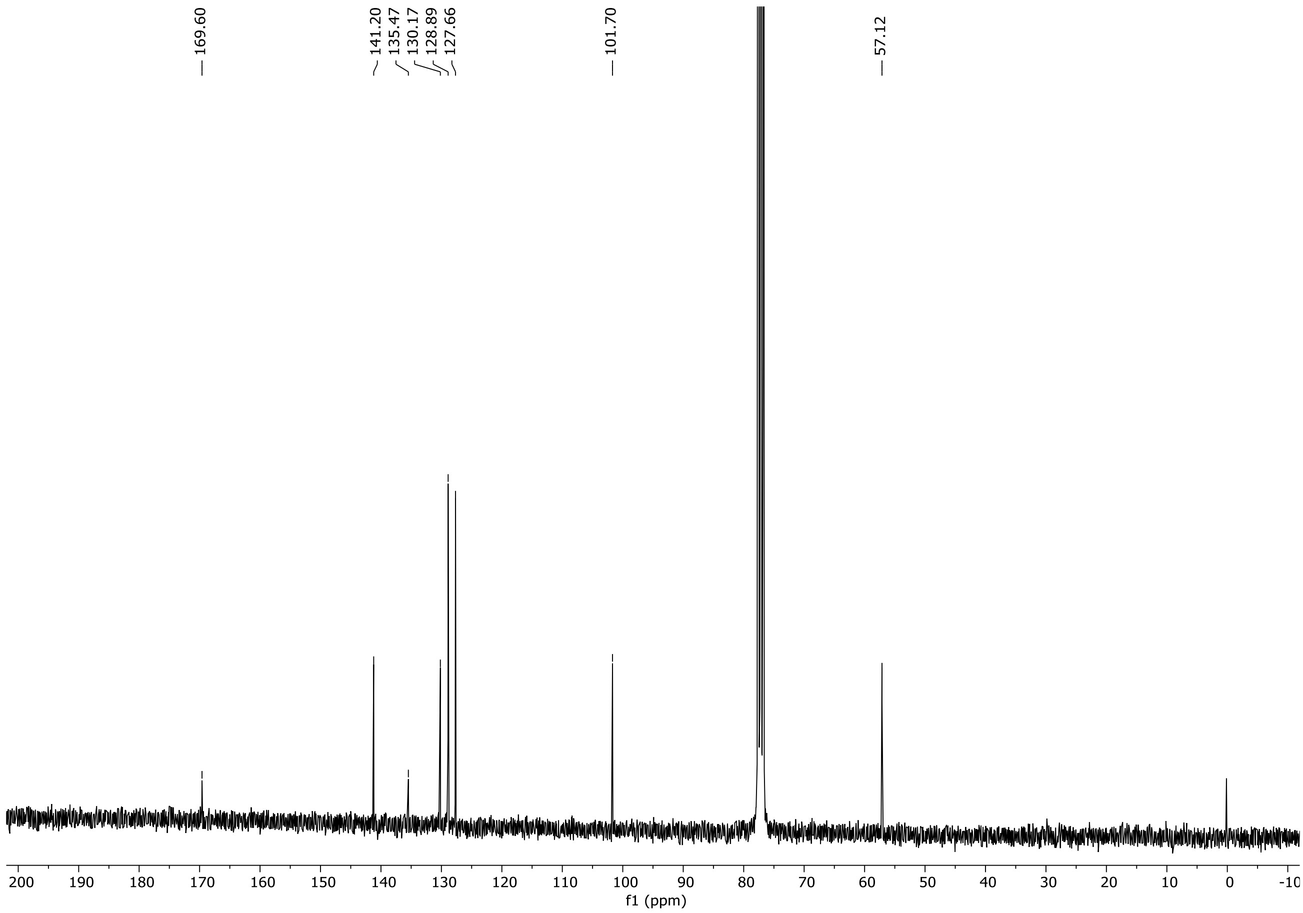
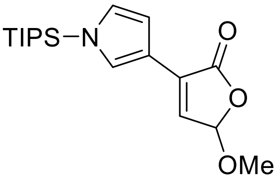


Figure S24. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **(±)-2e**.



(±)-2f

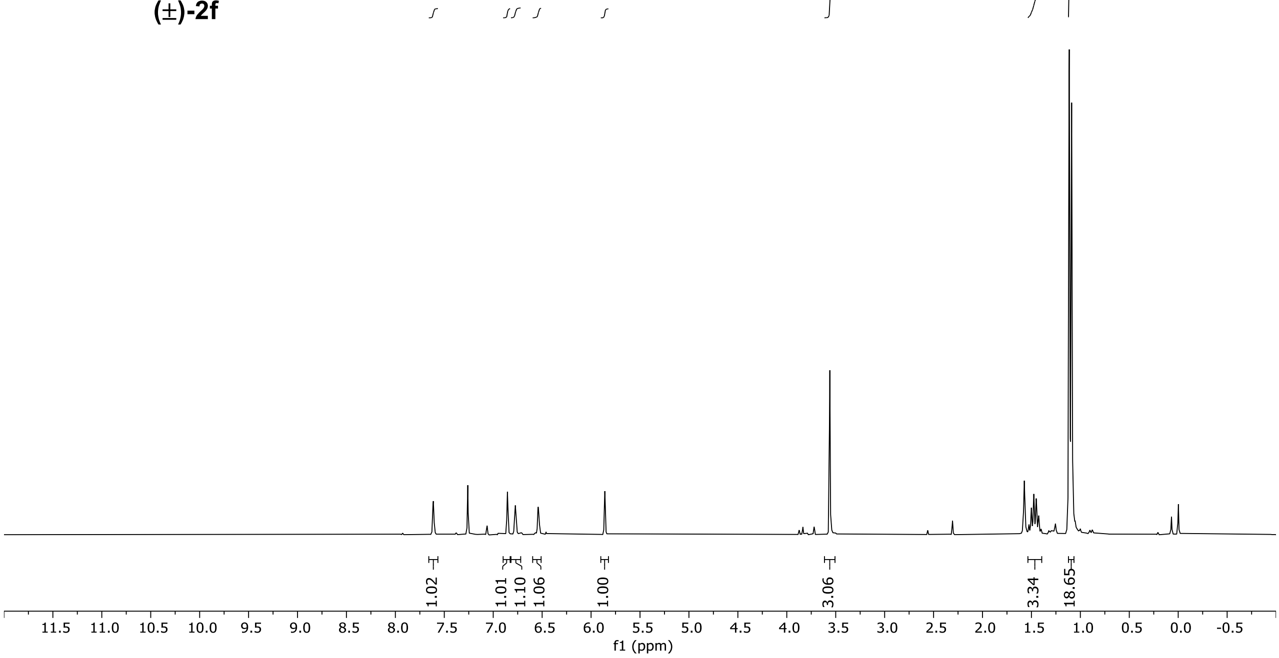


Figure S25. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **(±)-2f**.

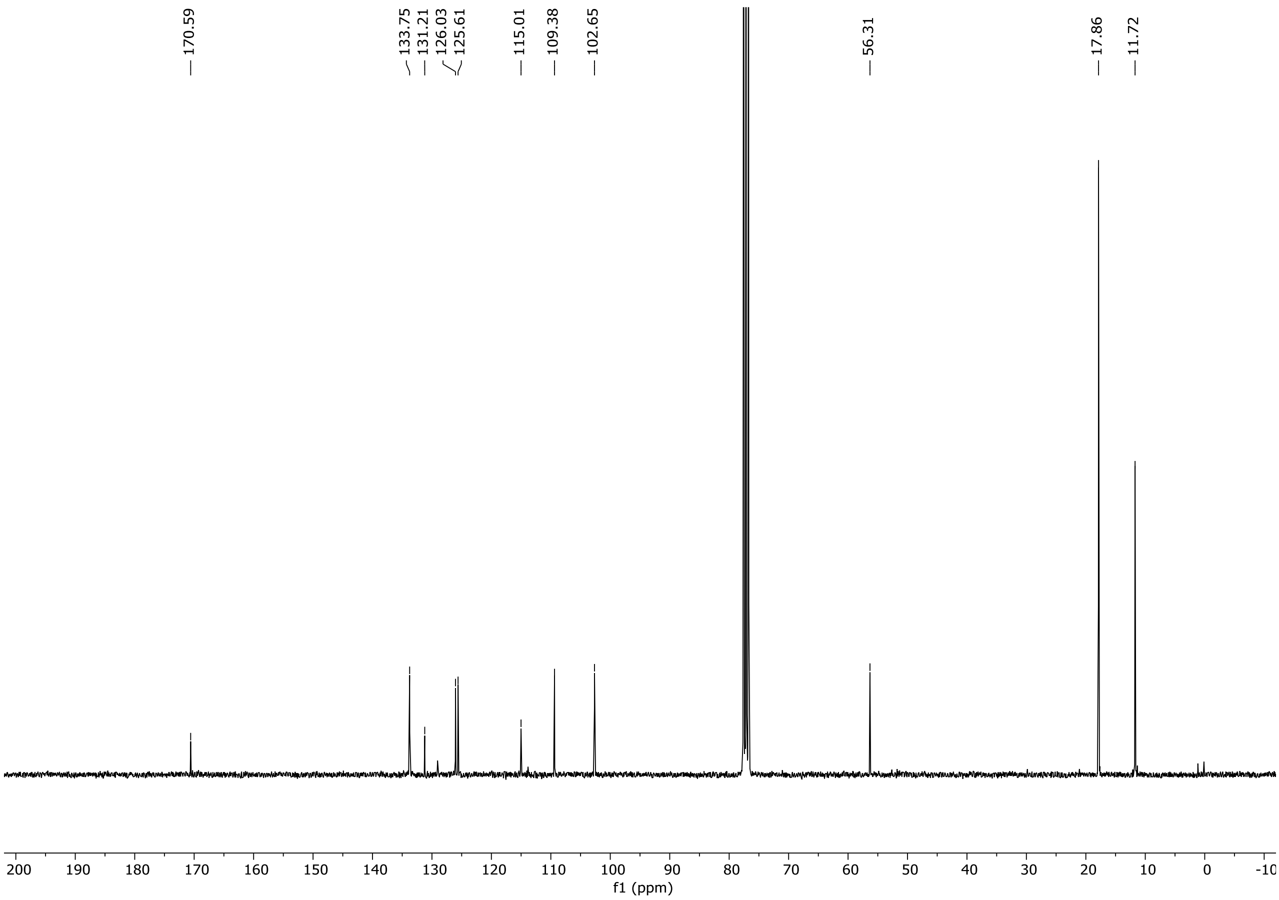
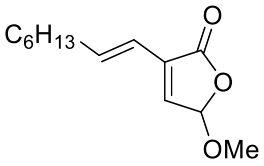


Figure S26. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **(±)-2f**.



(±)-2g

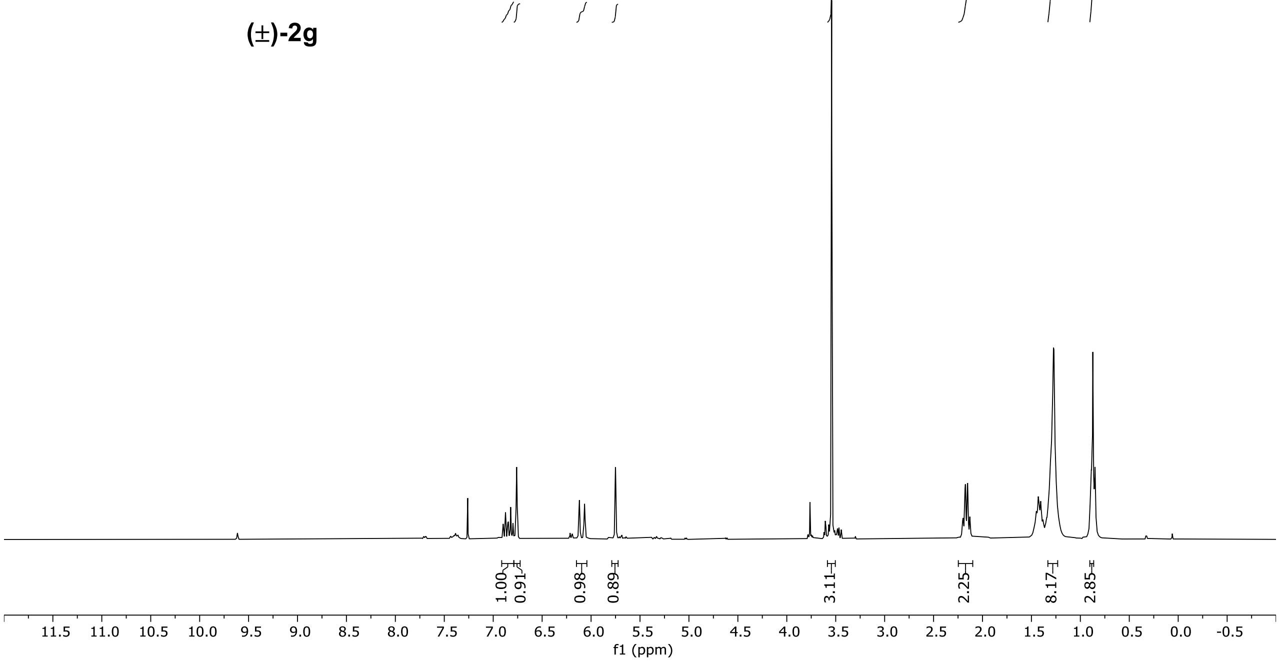


Figure S27. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **(±)-2g**.

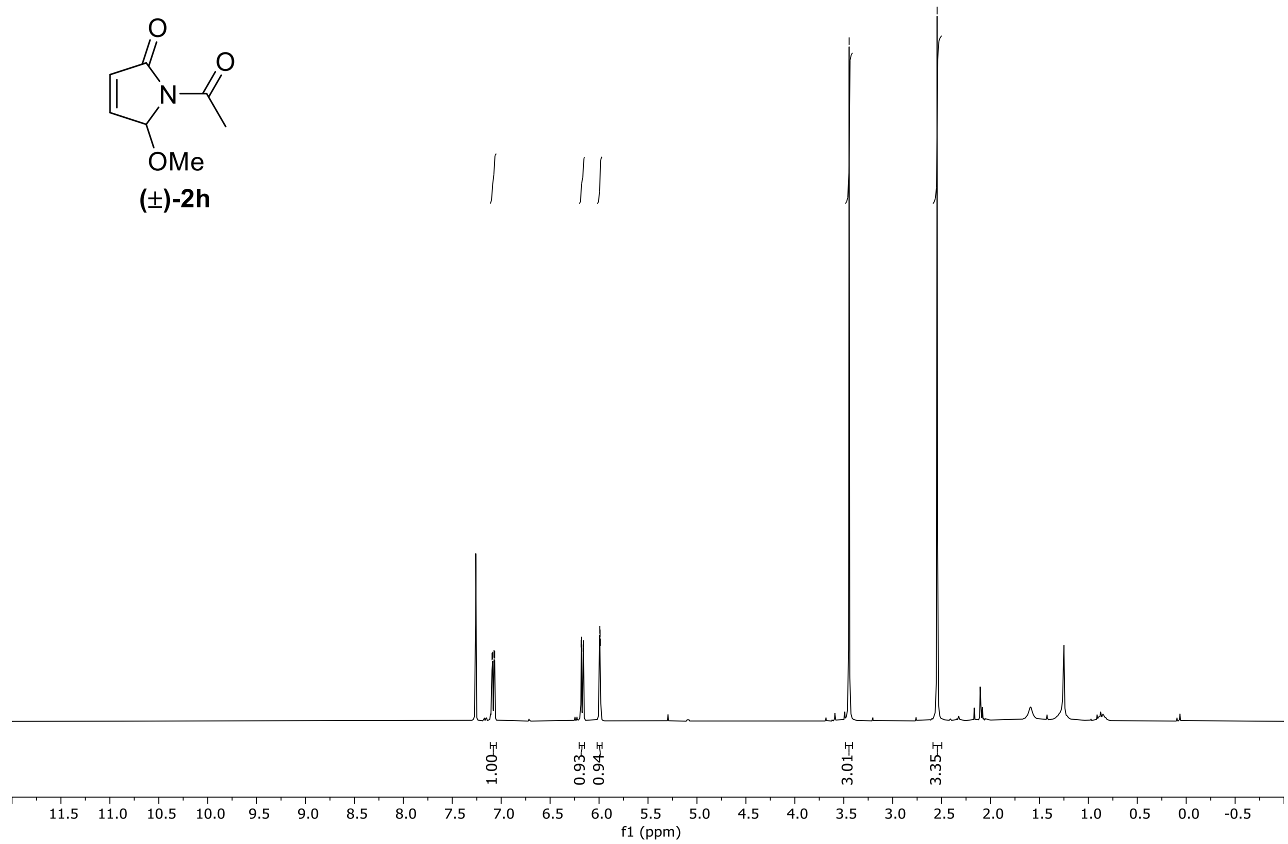


Figure S28. [1]H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **(±)-2h**.

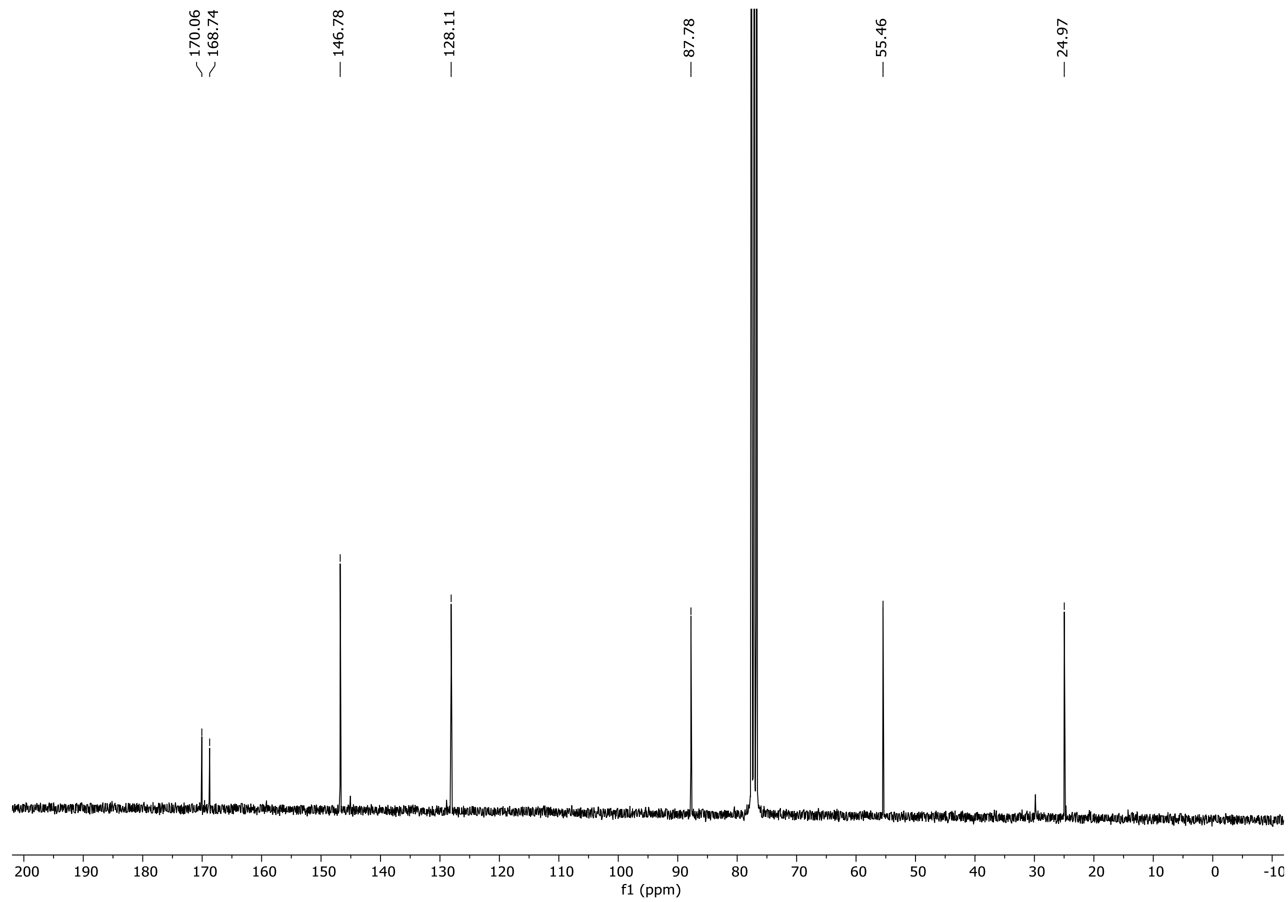


Figure S29. [13]C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **(±)-2h**.

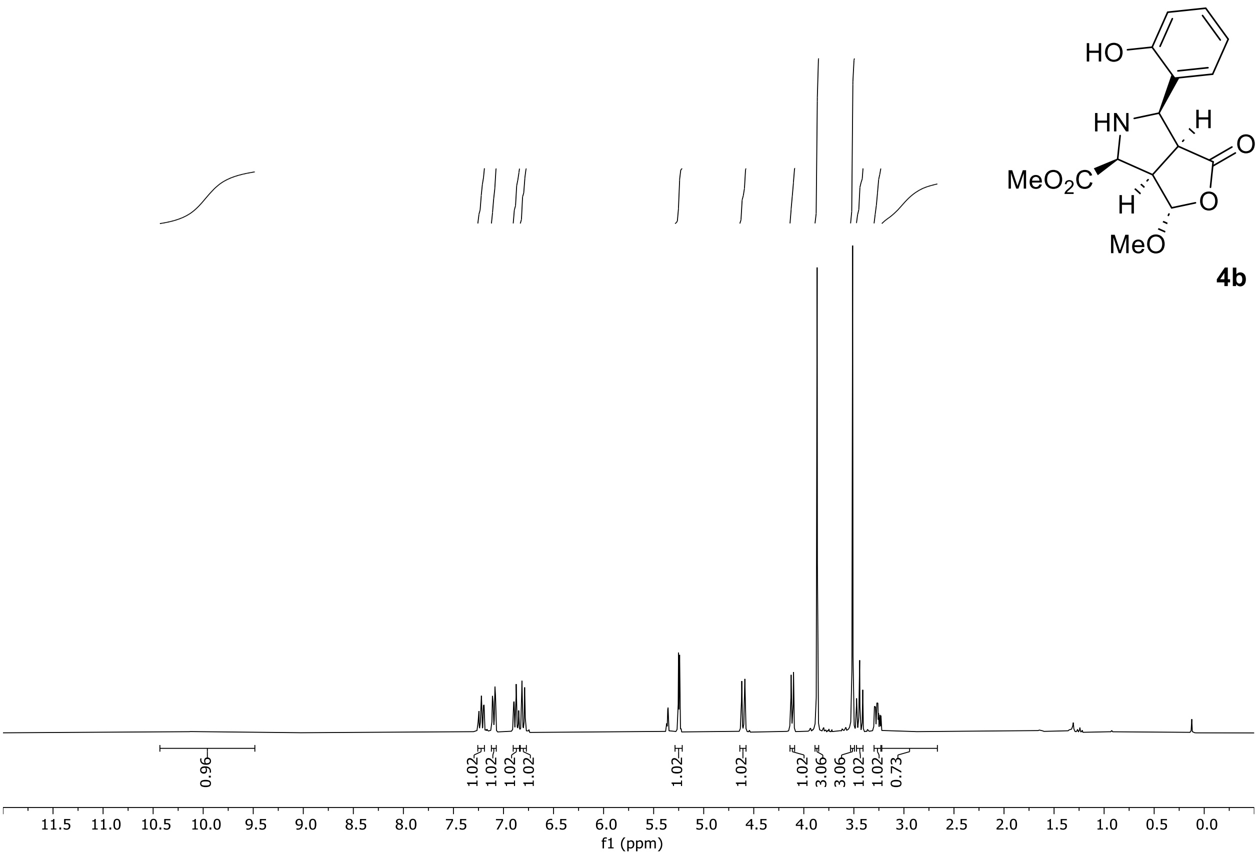


Figure S30. ^{1}H NMR spectrum (300 MHz, 298K, CD_2Cl_2) of **4b**.

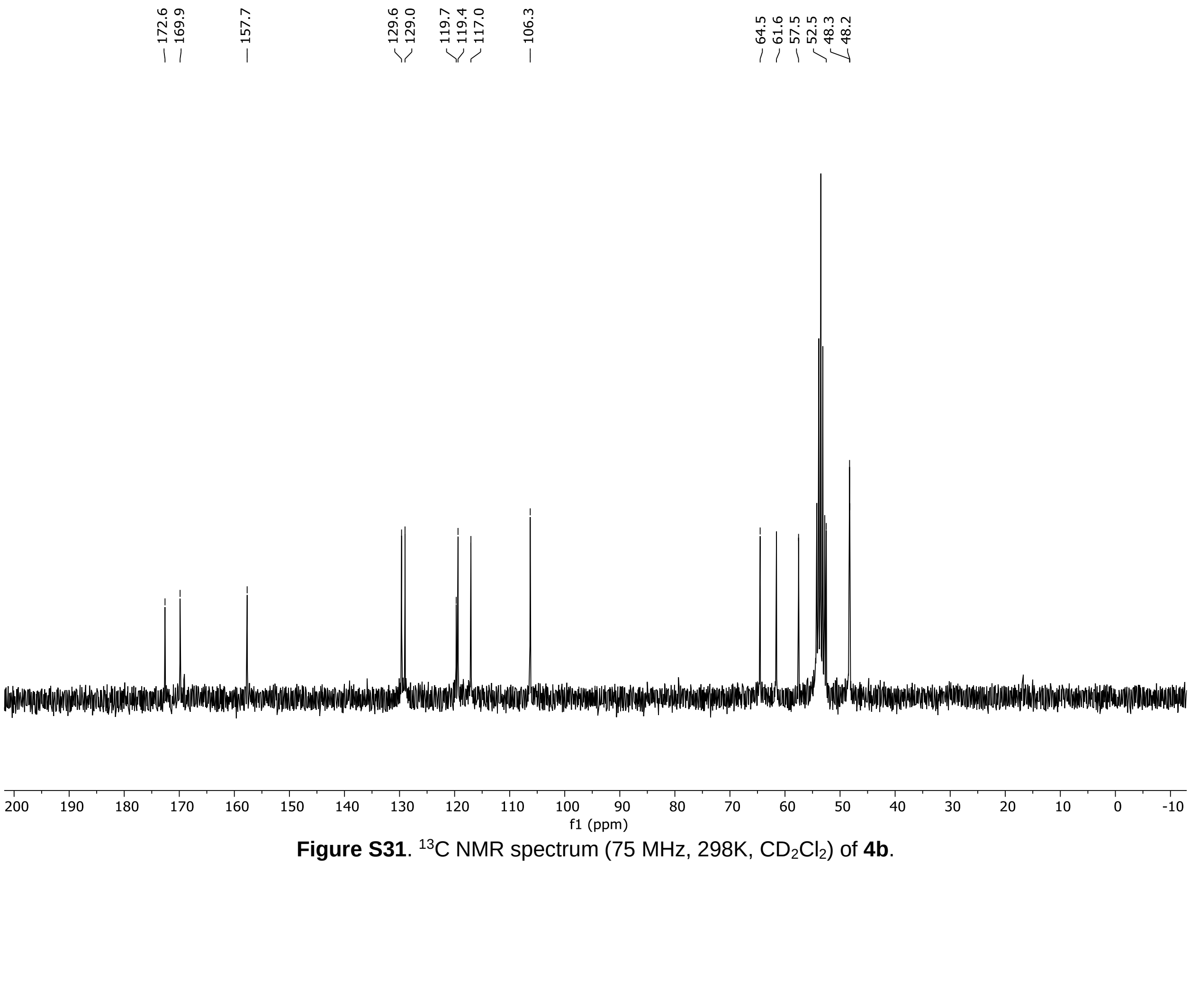


Figure S31. ^{13}C NMR spectrum (75 MHz, 298K, CD_2Cl_2) of **4b**.

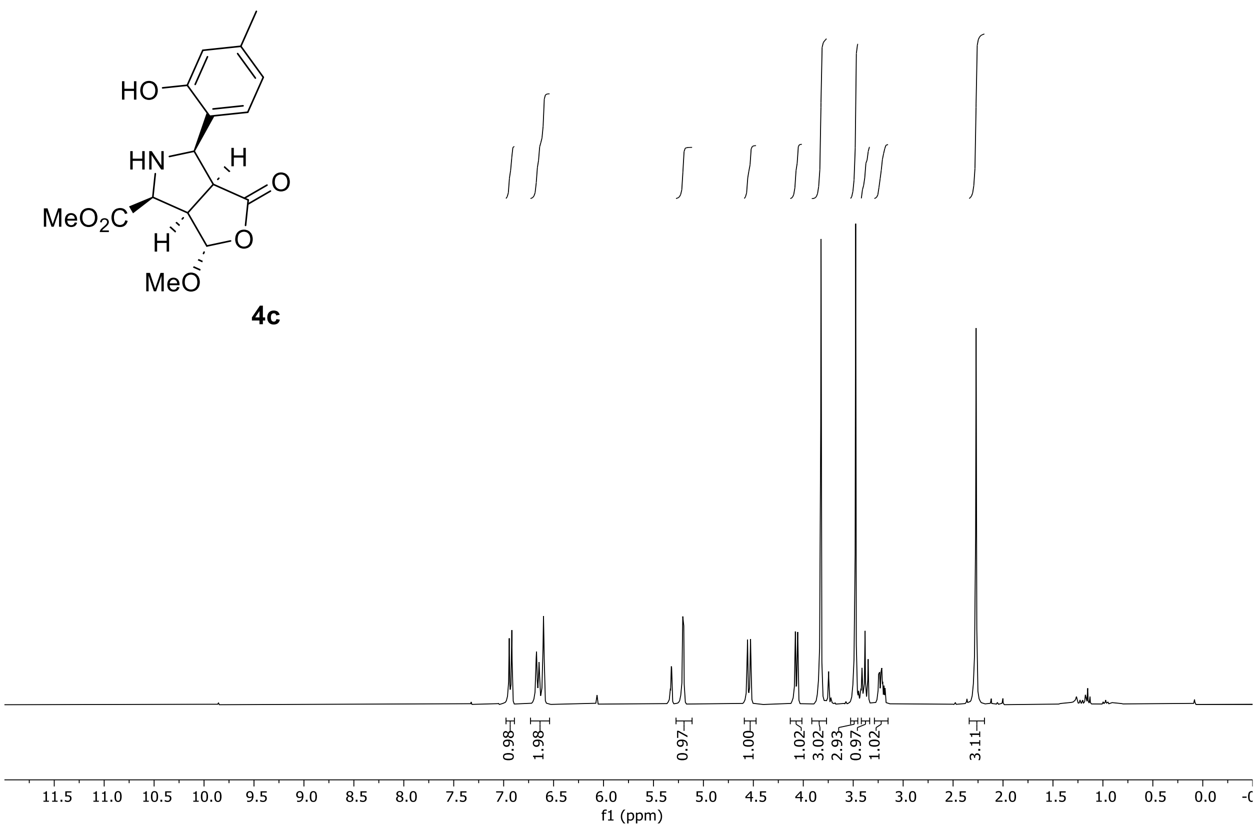


Figure S32. ^{1}H NMR spectrum (300 MHz, 298K, CD_2Cl_2) of **4c**.

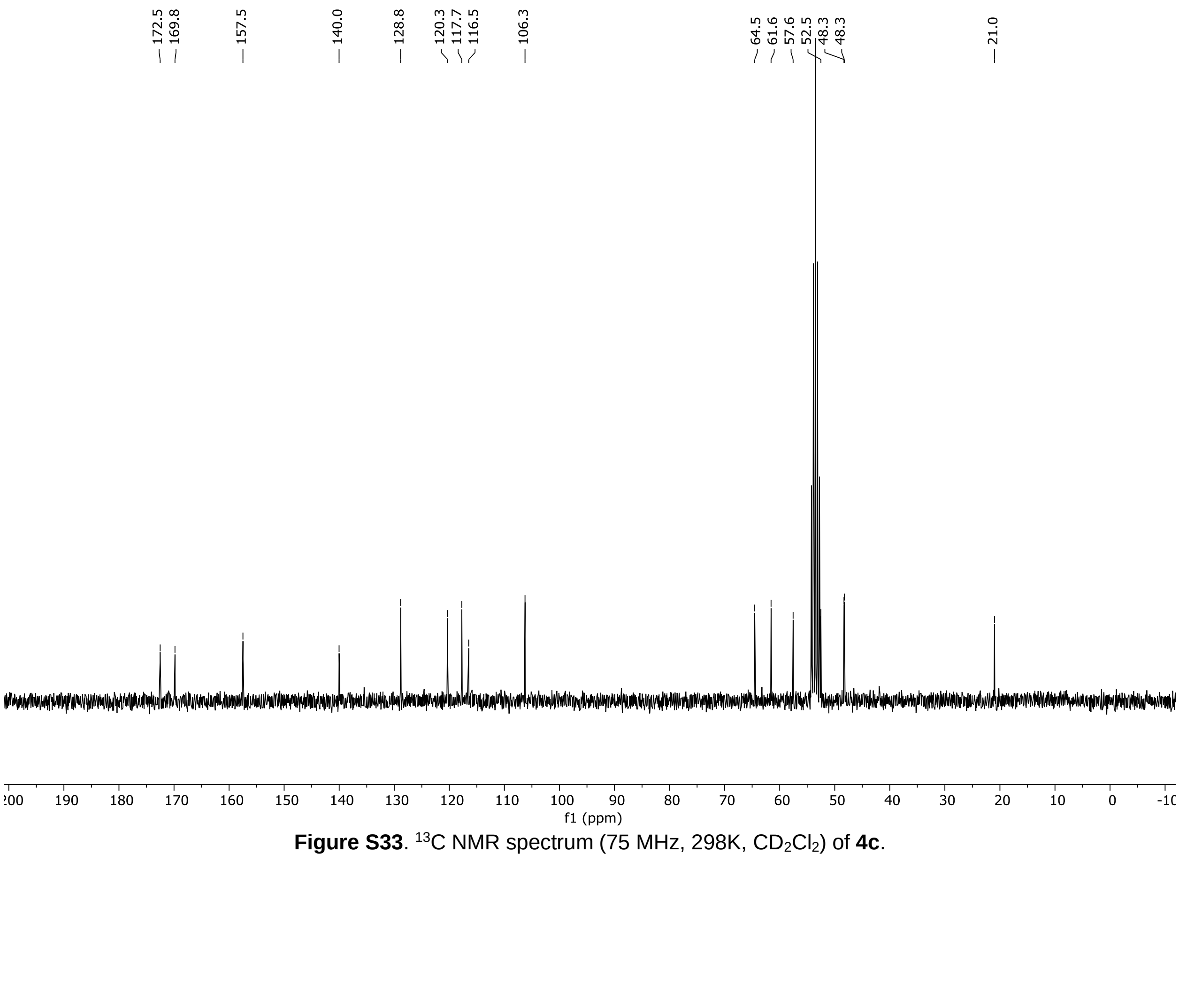


Figure S33. ^{13}C NMR spectrum (75 MHz, 298K, CD_2Cl_2) of **4c**.

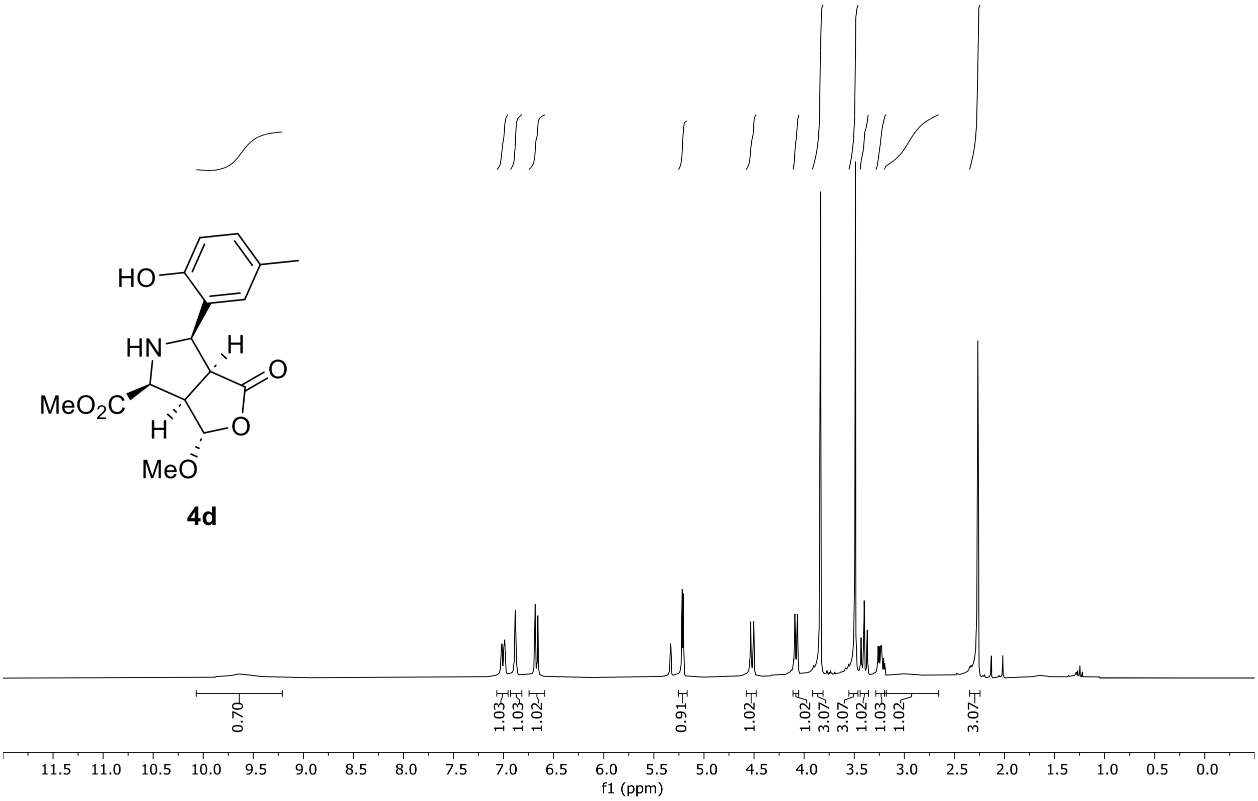


Figure S34. ^{1}H NMR spectrum (300 MHz, 298K, CD_2Cl_2) of **4d**.

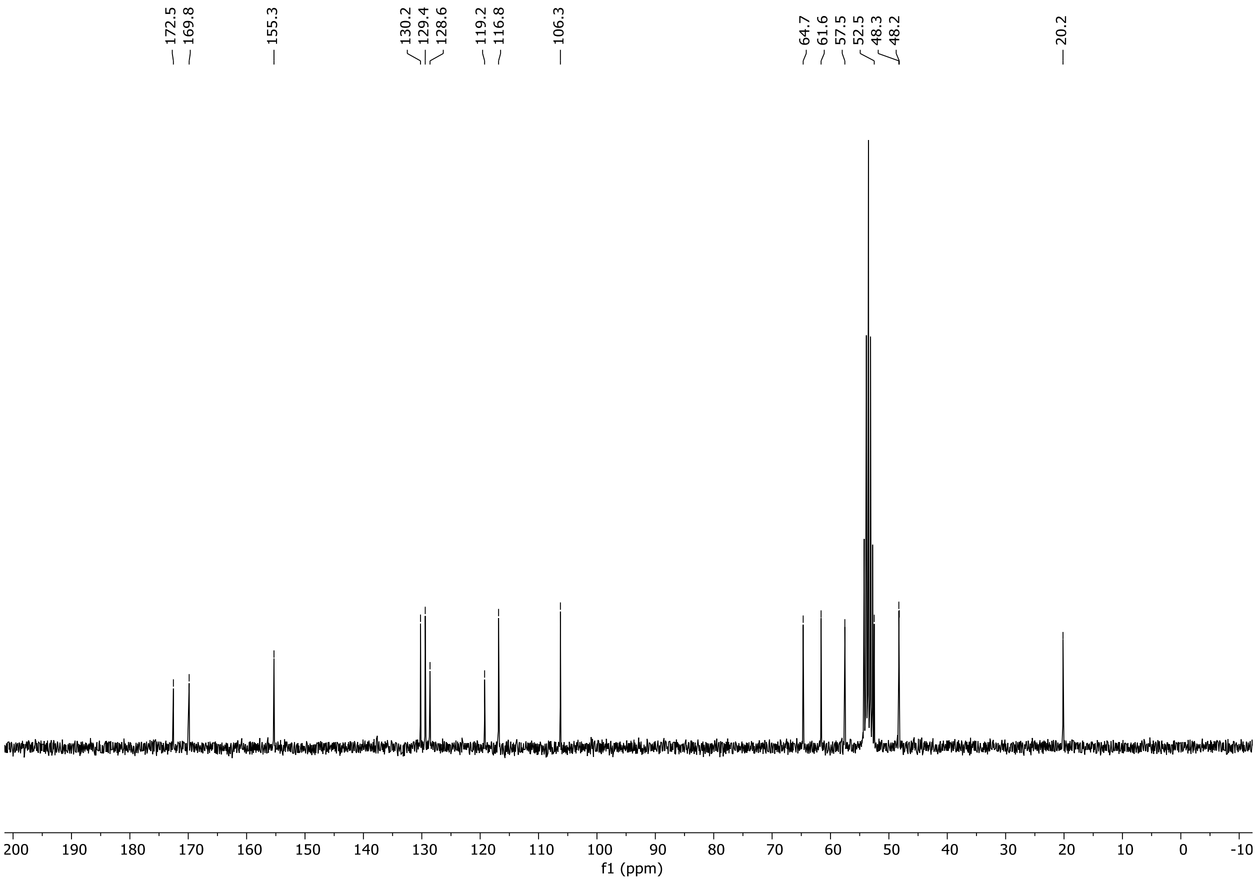


Figure S35. ^{13}C NMR spectrum (75 MHz, 298K, CD_2Cl_2) of **4d**.

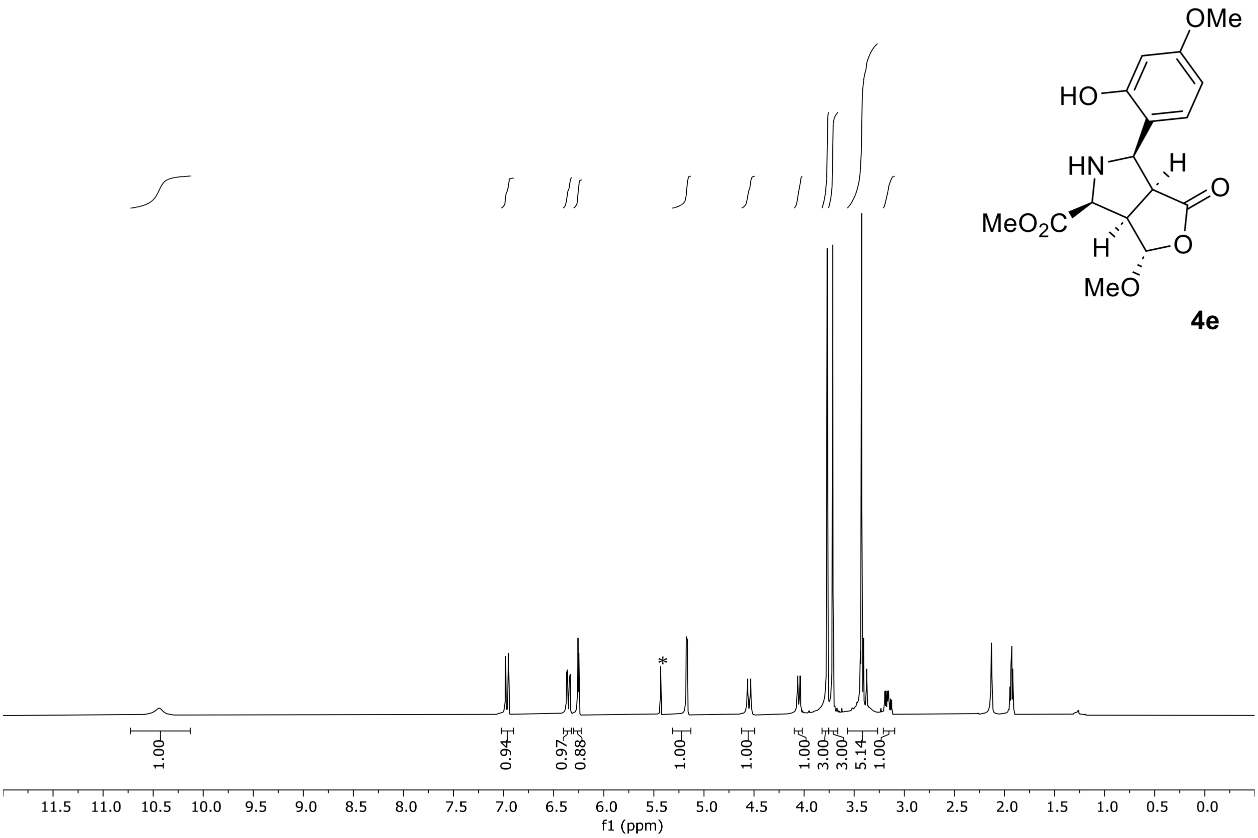


Figure S36. ^{1}H NMR spectrum (300 MHz, 298K, CD_3CN) of **4e** ($^{*}CH_2Cl_2$ solvent peak).

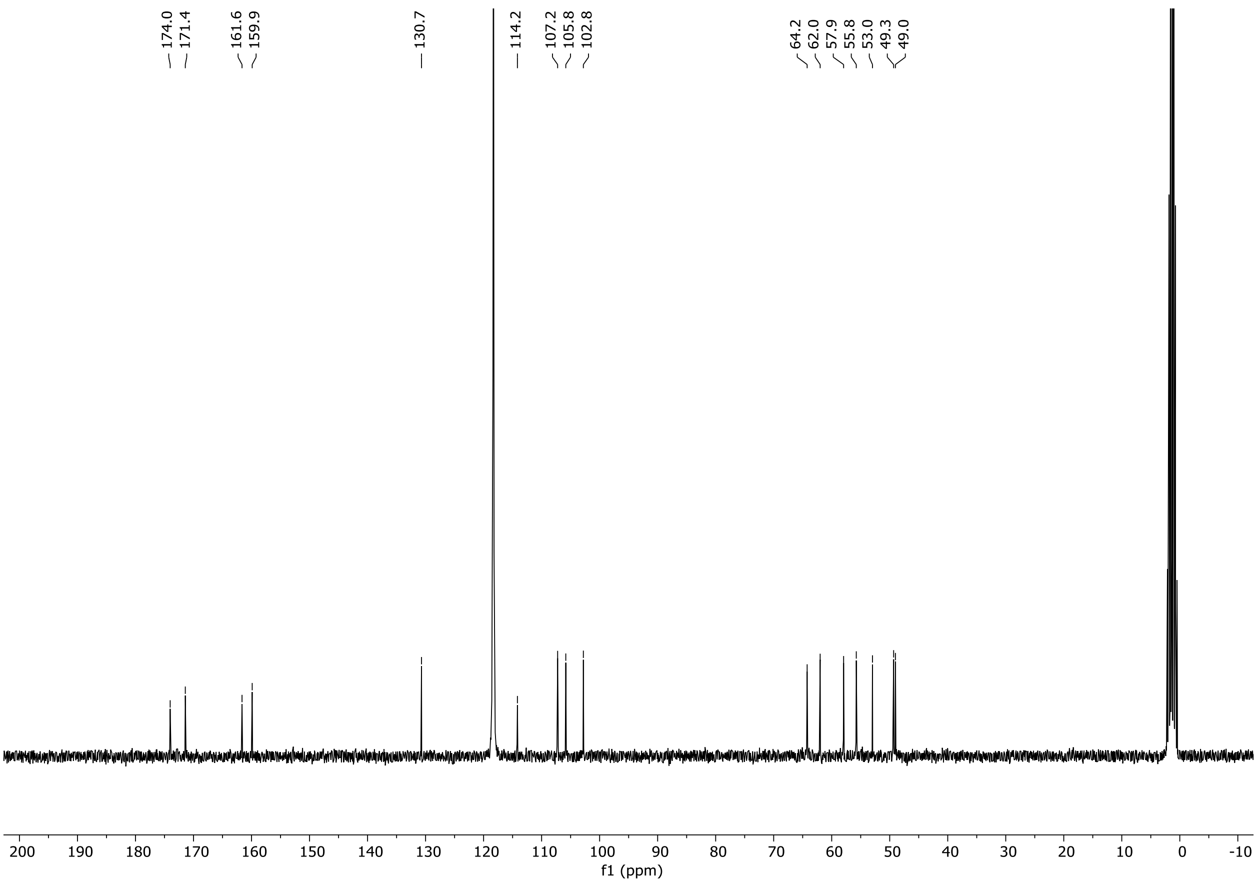
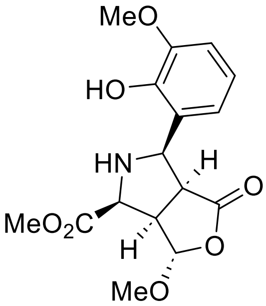


Figure S37. ^{13}C NMR spectrum (75 MHz, 298K, CD_3CN) of **4e**.



4f

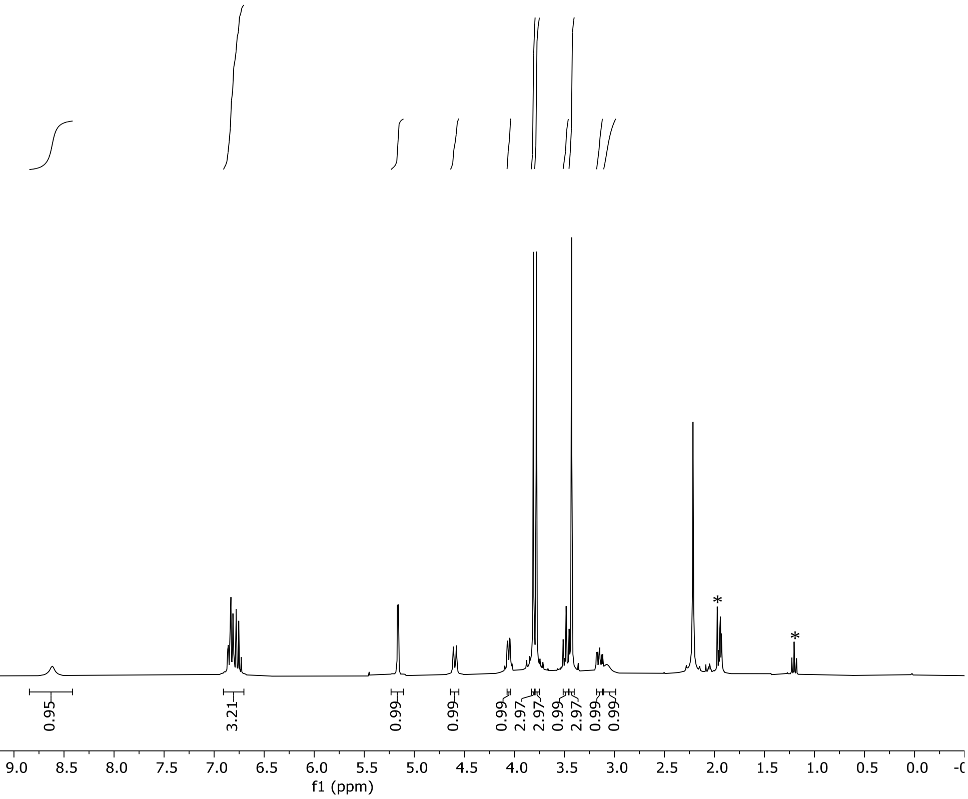


Figure S38. ^{1}H NMR spectrum (300 MHz, 298K, CD_3CN) of **4f** (*AcOEt solvent peaks).

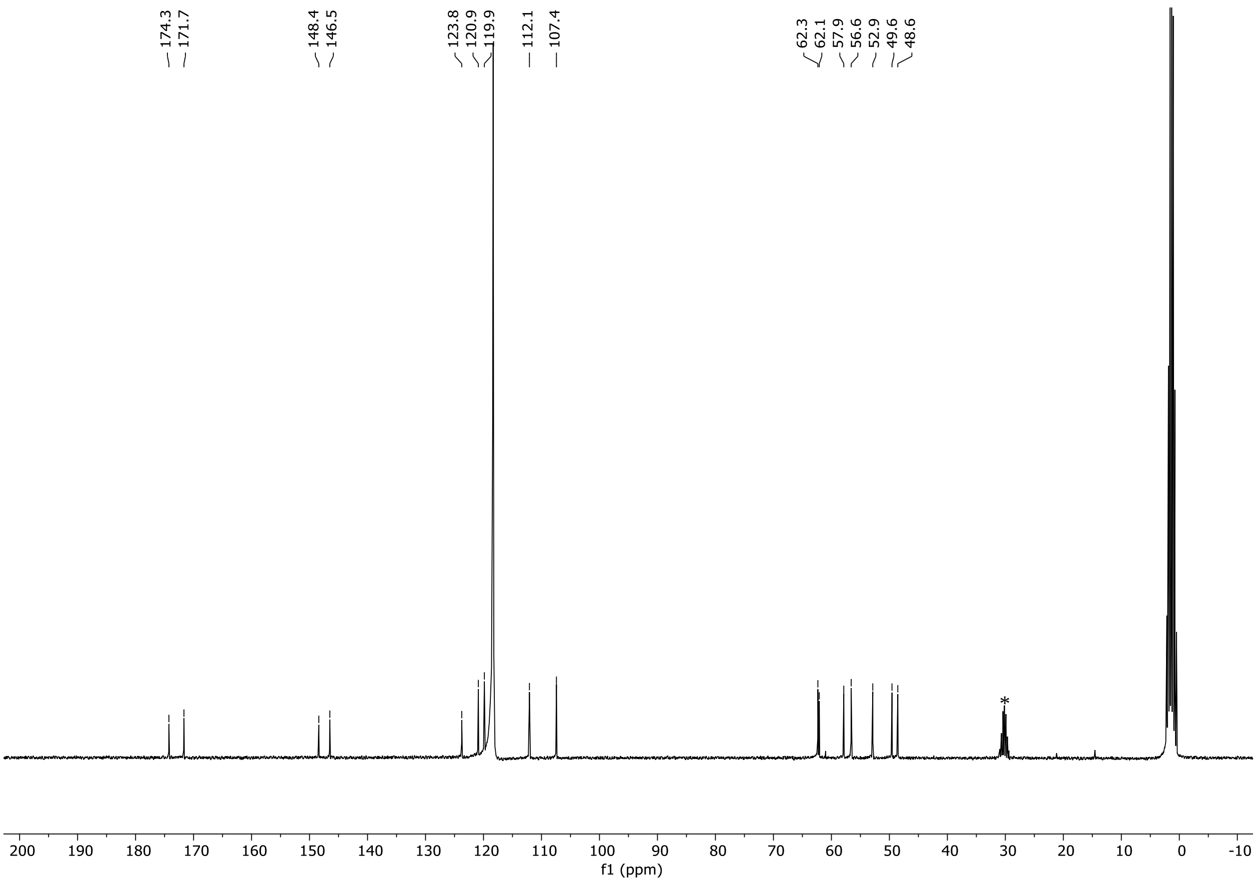
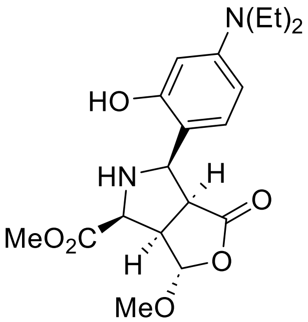


Figure S39. ^{13}C NMR spectrum (76 MHz, 298K, CD_3CN) of **4f** ($^{*}(CD_3)_2CO$ solvent peak).



4g

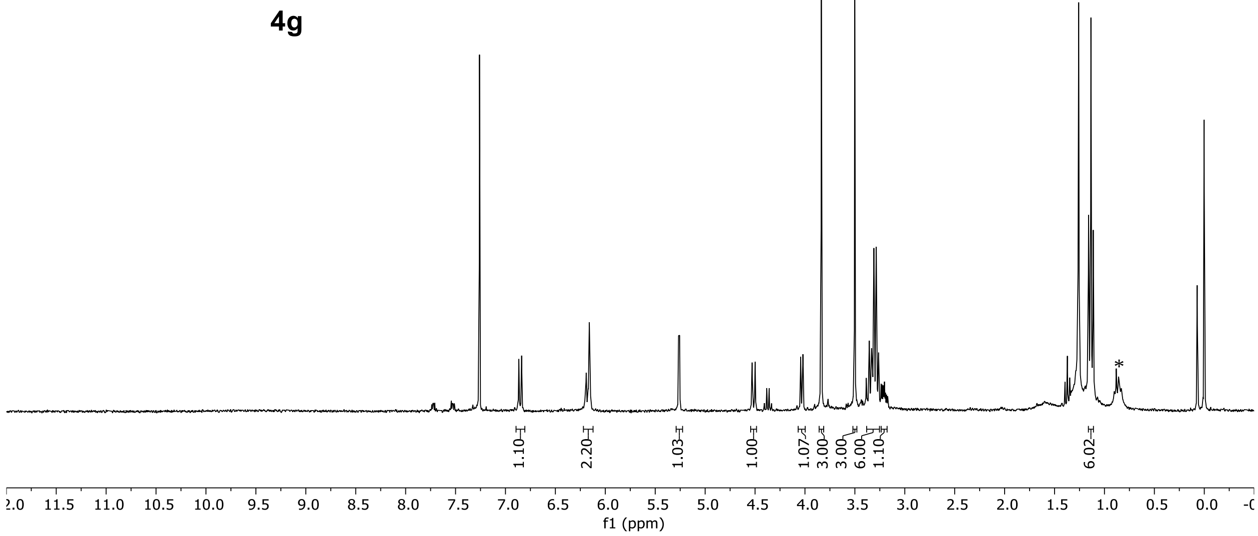


Figure S40. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **4g** (*grease peaks).

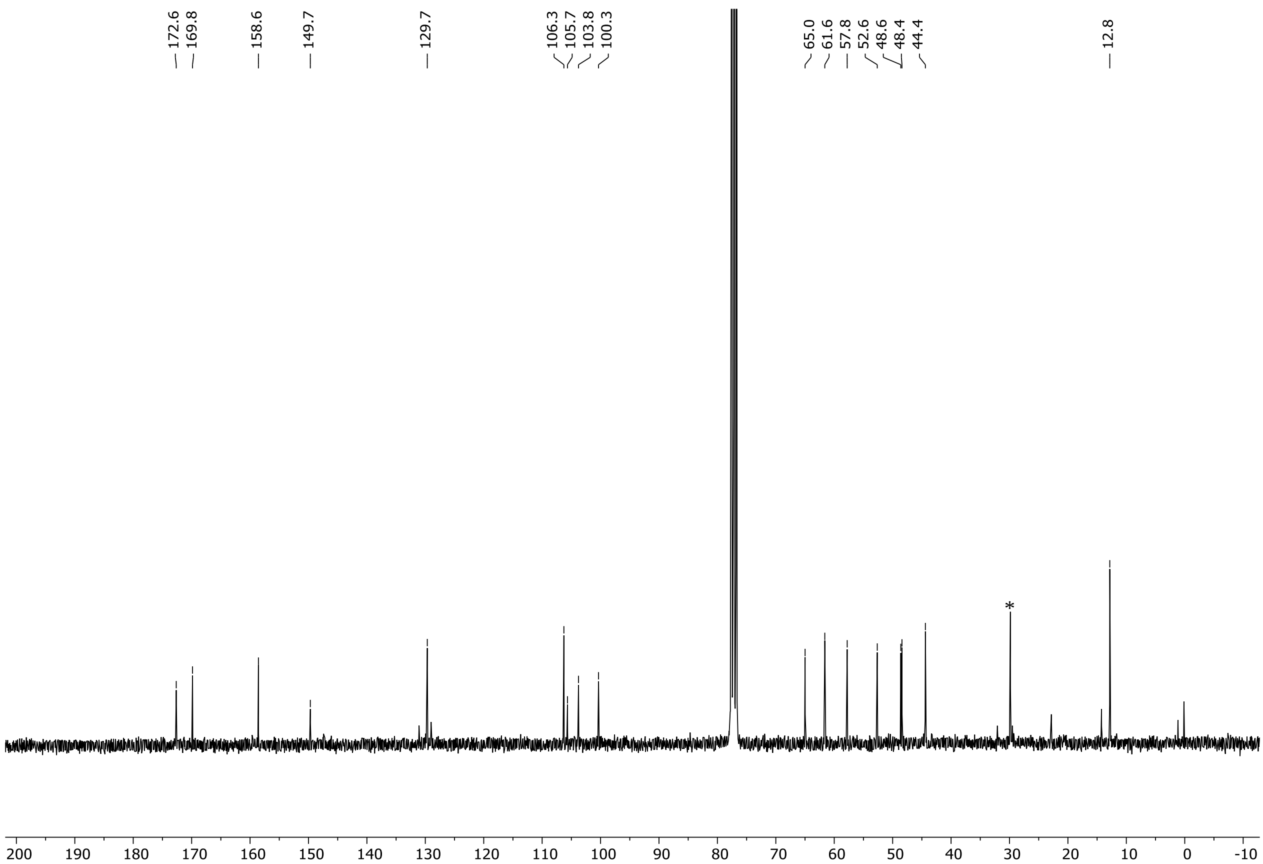
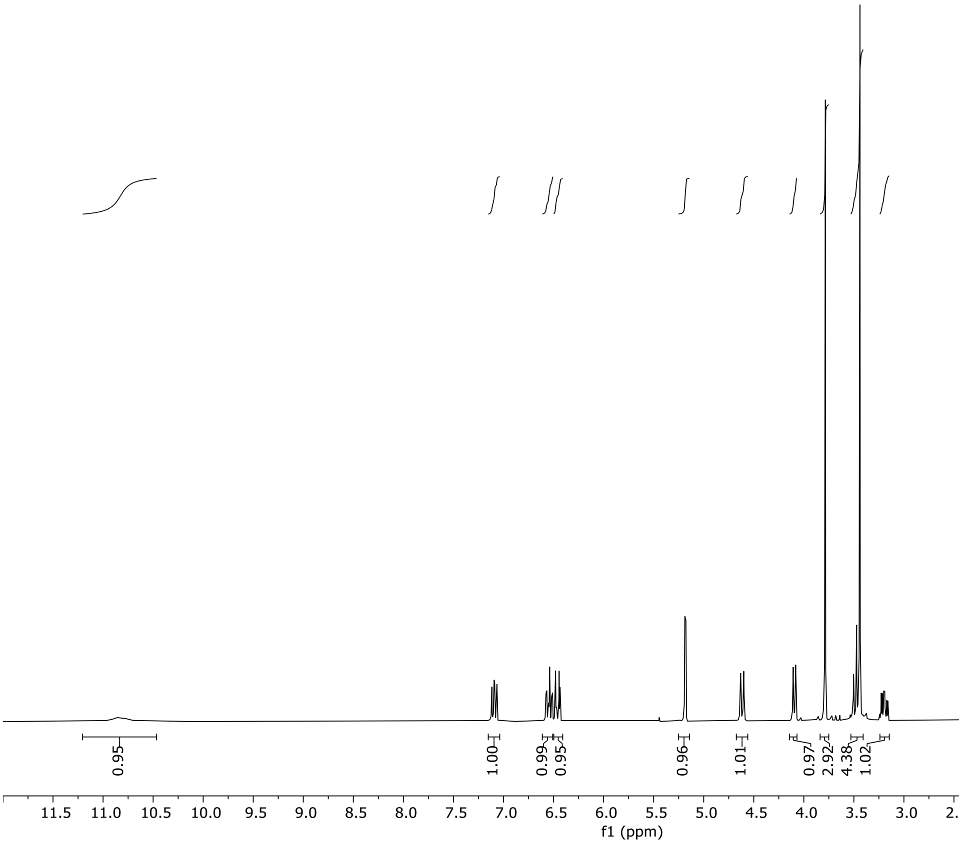
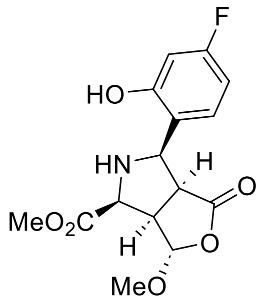


Figure S41. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **4g** (*grease peak).





4h

Figure S42. ^{1}H NMR spectrum (300 MHz, 298K, CD_3CN) of 4h.

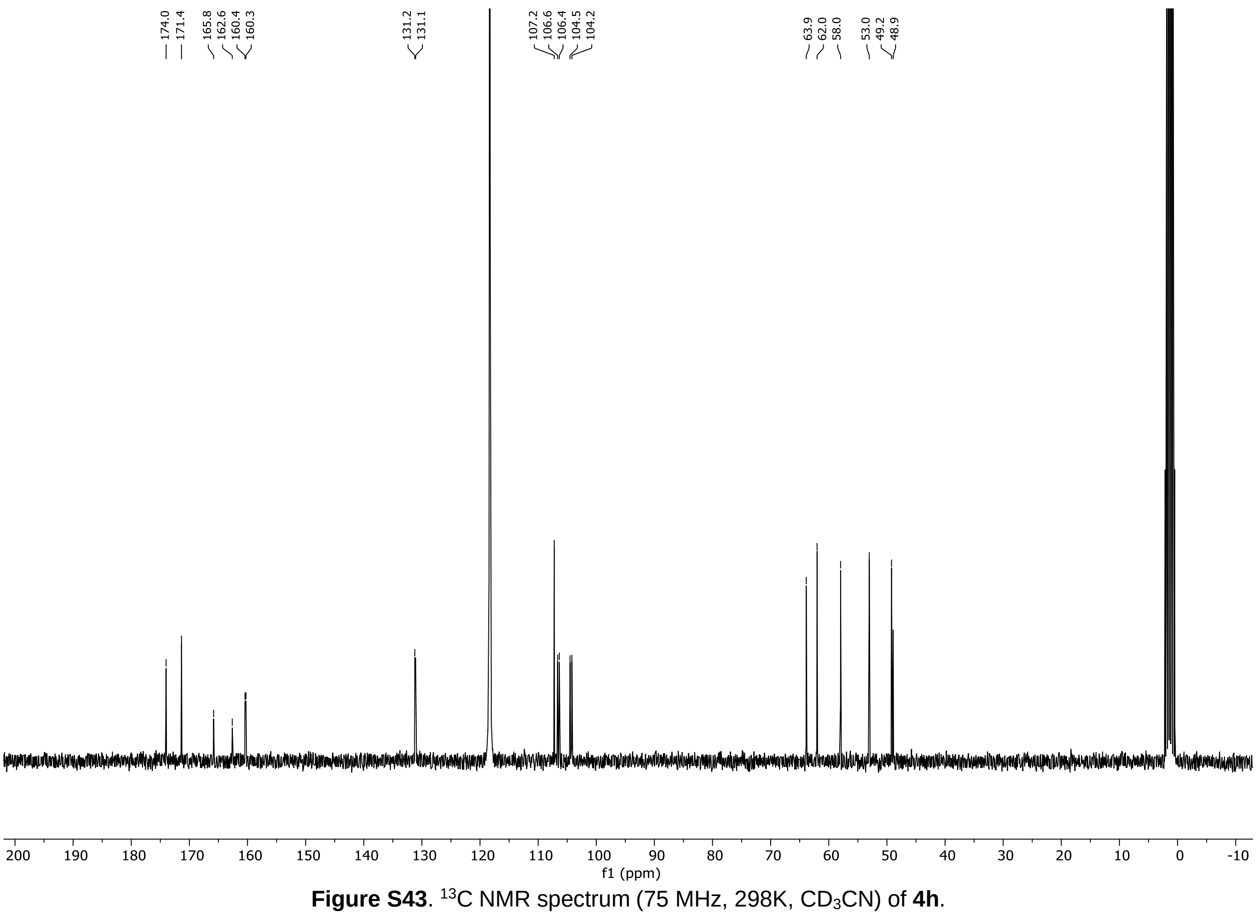


Figure S43. ^{13}C NMR spectrum (75 MHz, 298K, CD_3CN) of 4h.

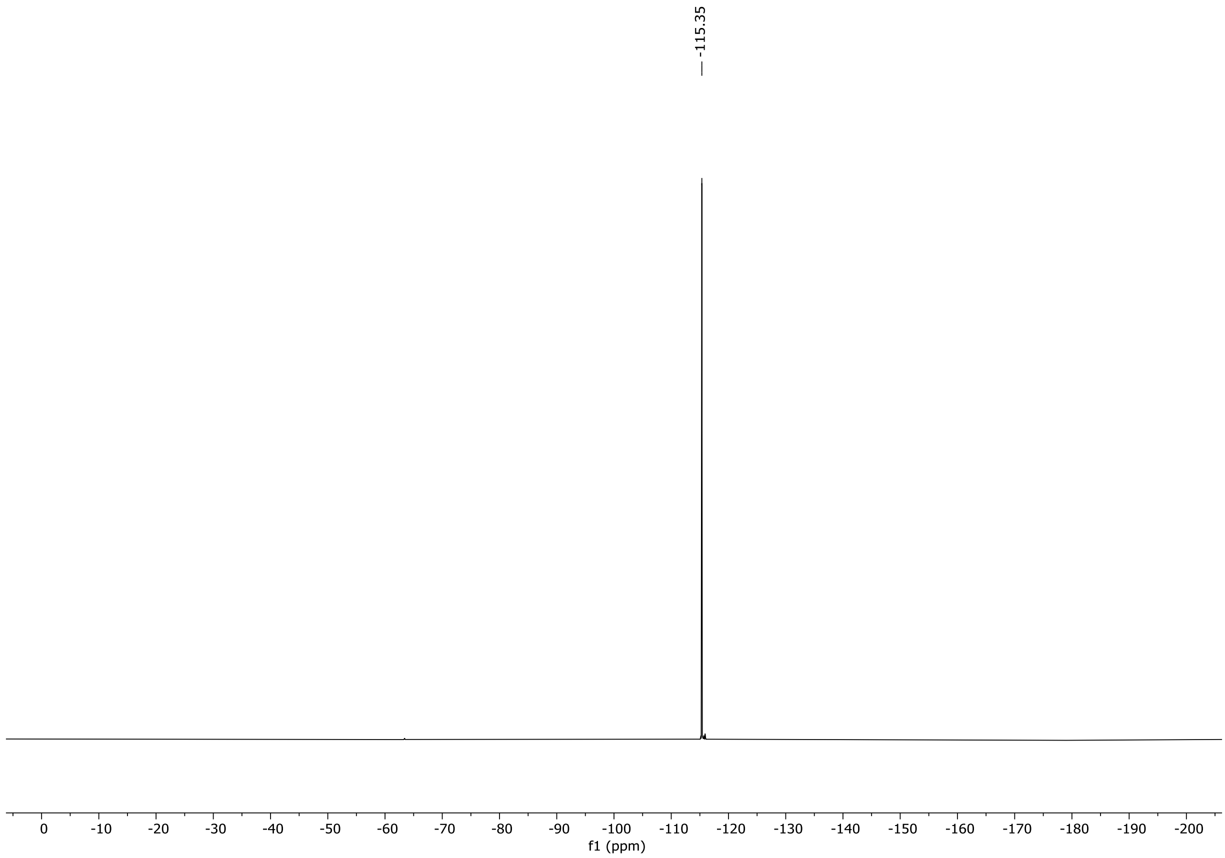


Figure S44. ^{19}F NMR spectrum (75 MHz, 298K, CD_3CN) of **4h**.

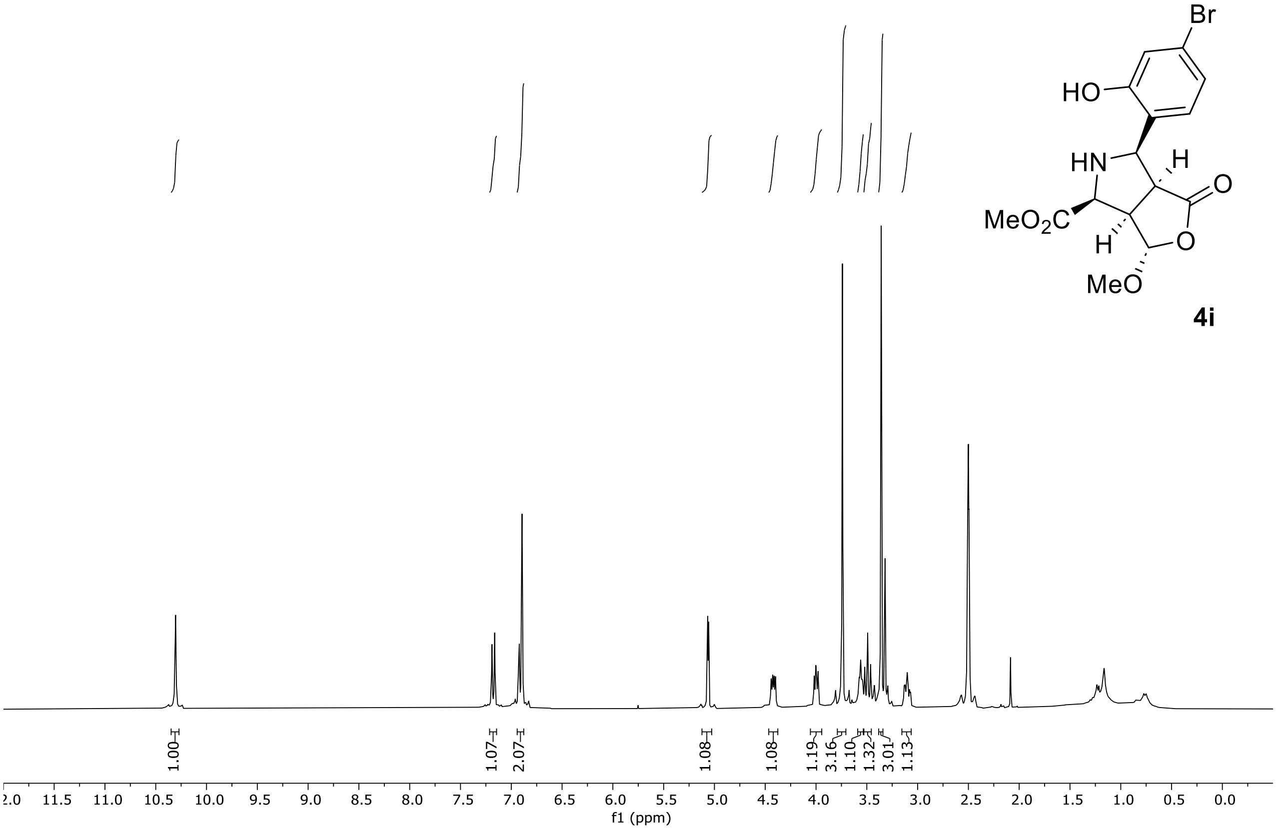


Figure S45. ^{1}H NMR spectrum (300 MHz, 298K, $(CD_3)_2SO$) of **4i**.

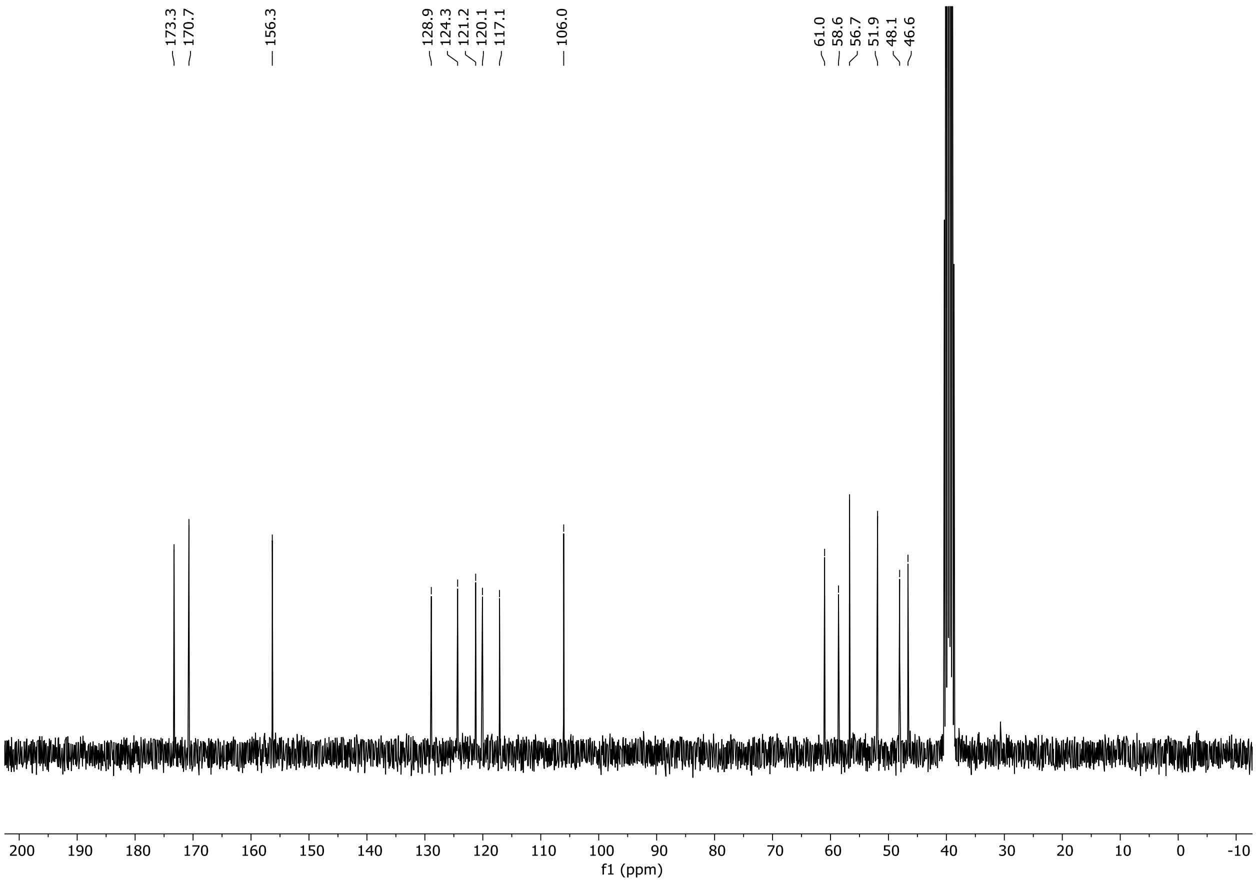


Figure S46. ^{13}C NMR spectrum (75 MHz, 298K, $(CD_3)_2SO$) of **4i**.

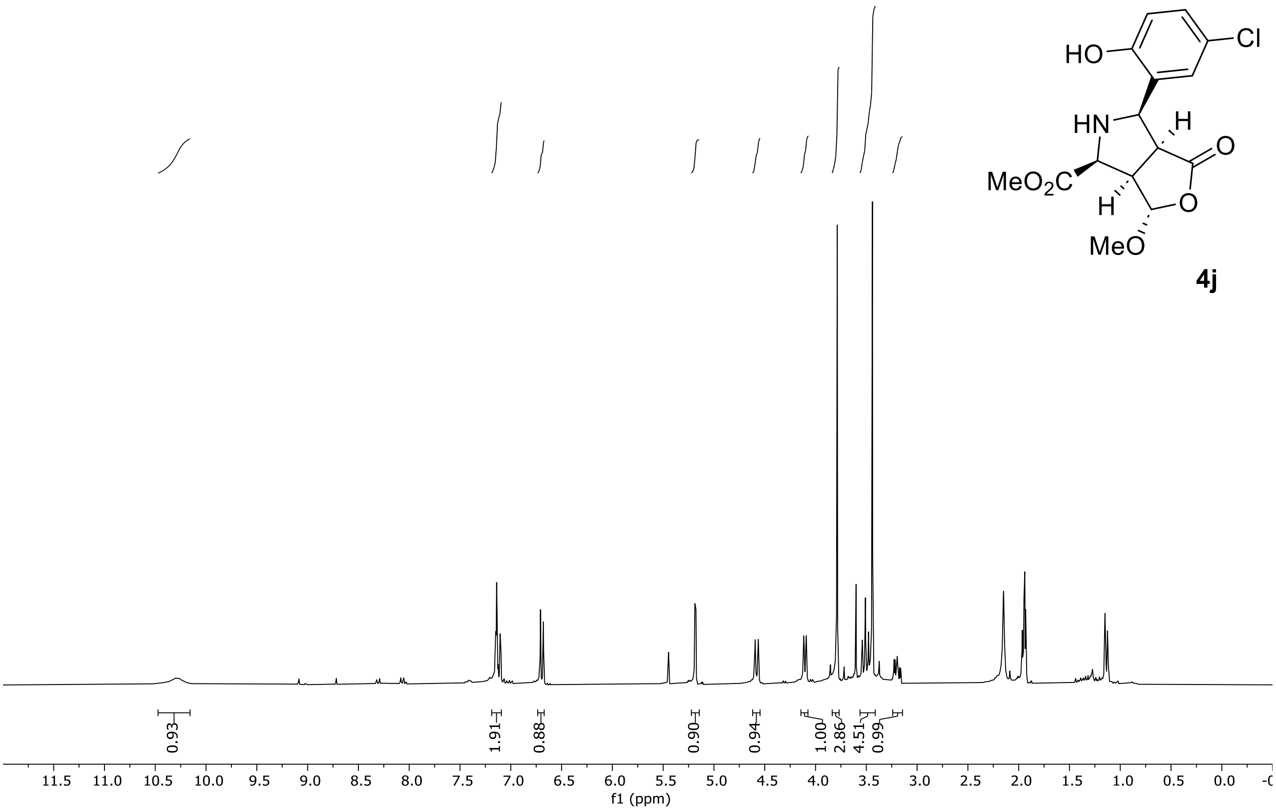


Figure S47. ^{1}H NMR spectrum (300 MHz, 298K, CD_3CN) of **4j**.

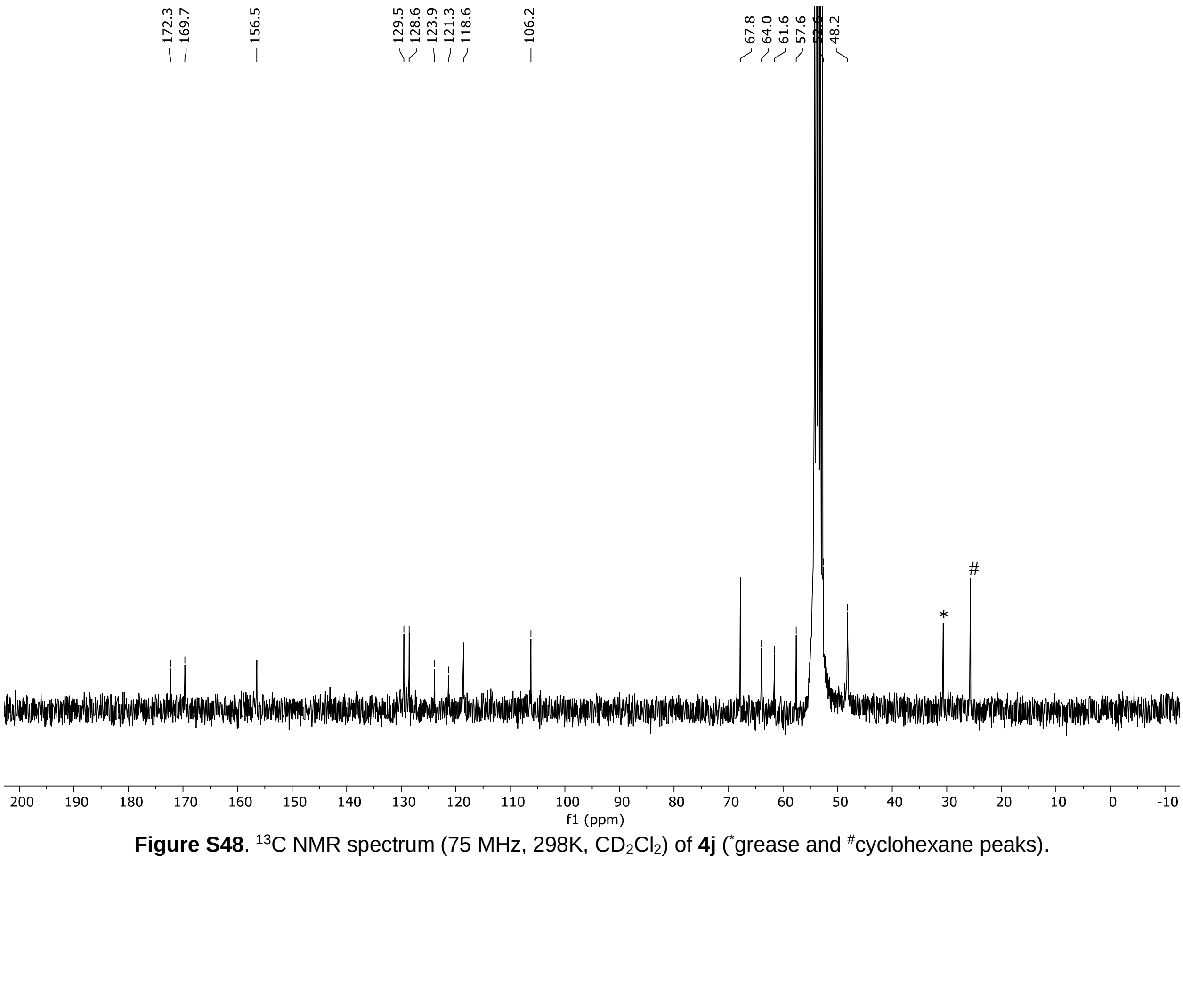


Figure S48. ^{13}C NMR spectrum (75 MHz, 298K, CD_2Cl_2) of **4j** (*grease and $^{\#}$cyclohexane peaks).

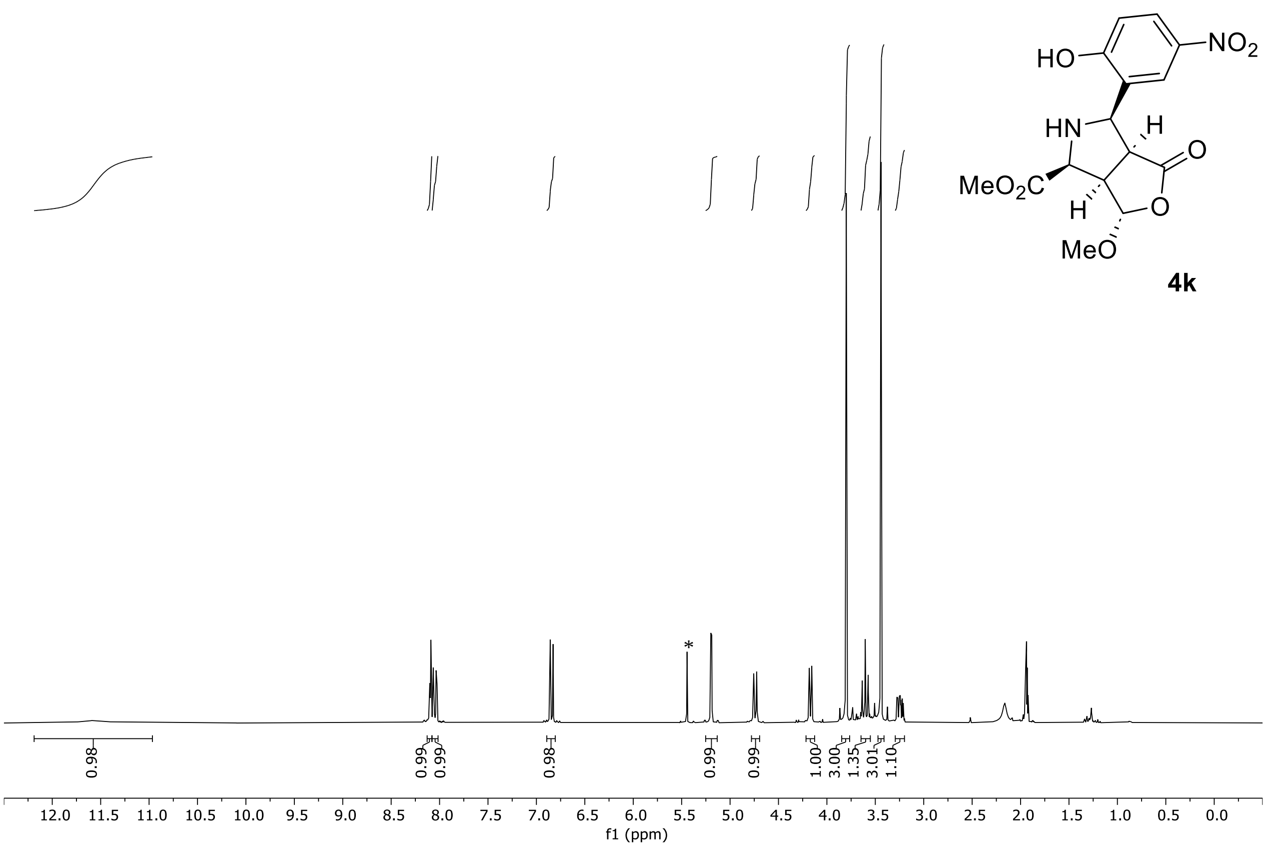


Figure S49. ^{1}H NMR spectrum (300 MHz, 298K, CD_3CN) of **4k** ($^{*}CH_2Cl_2$ solvent peak).

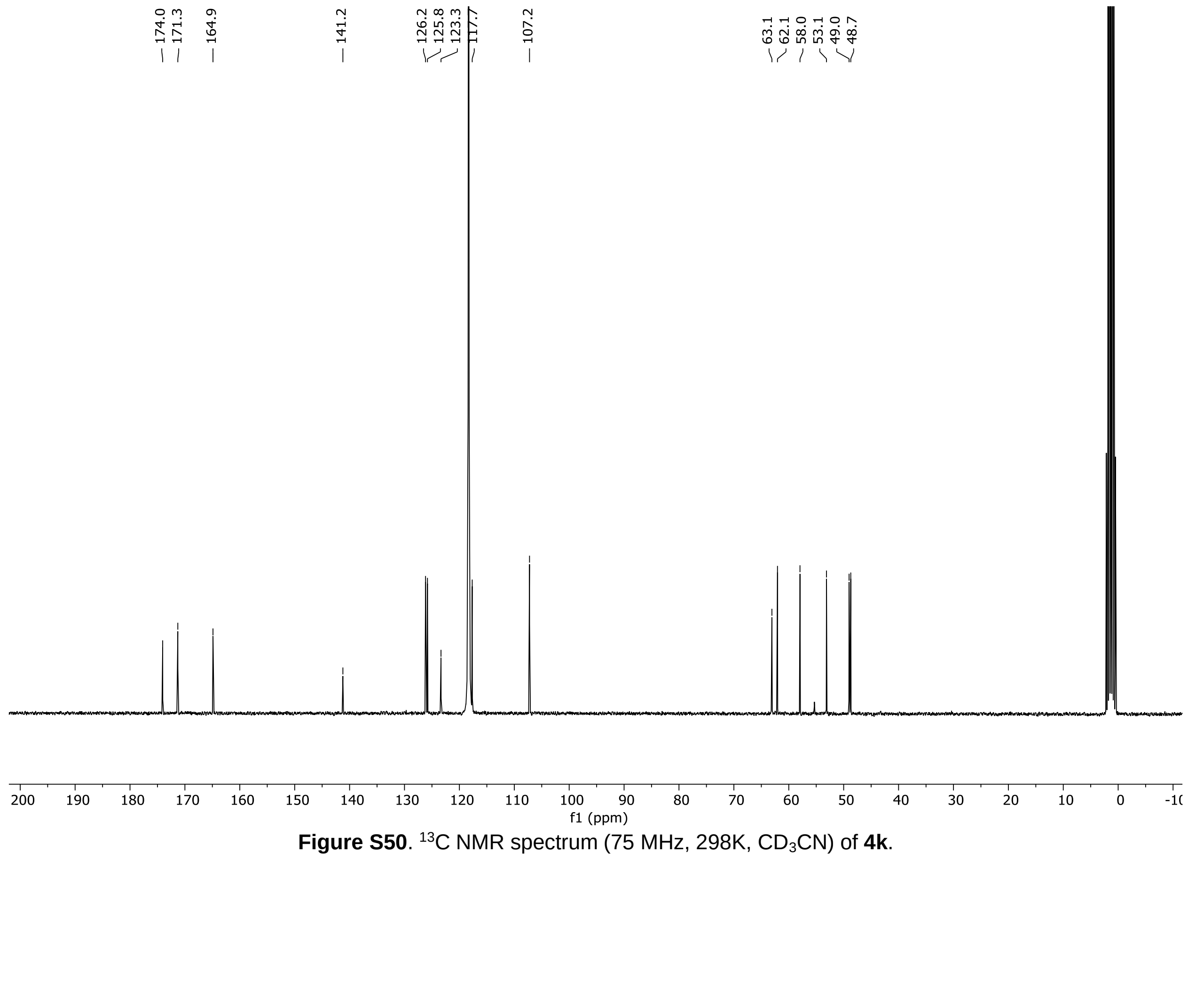


Figure S50. ^{13}C NMR spectrum (75 MHz, 298K, CD_3CN) of **4k**.

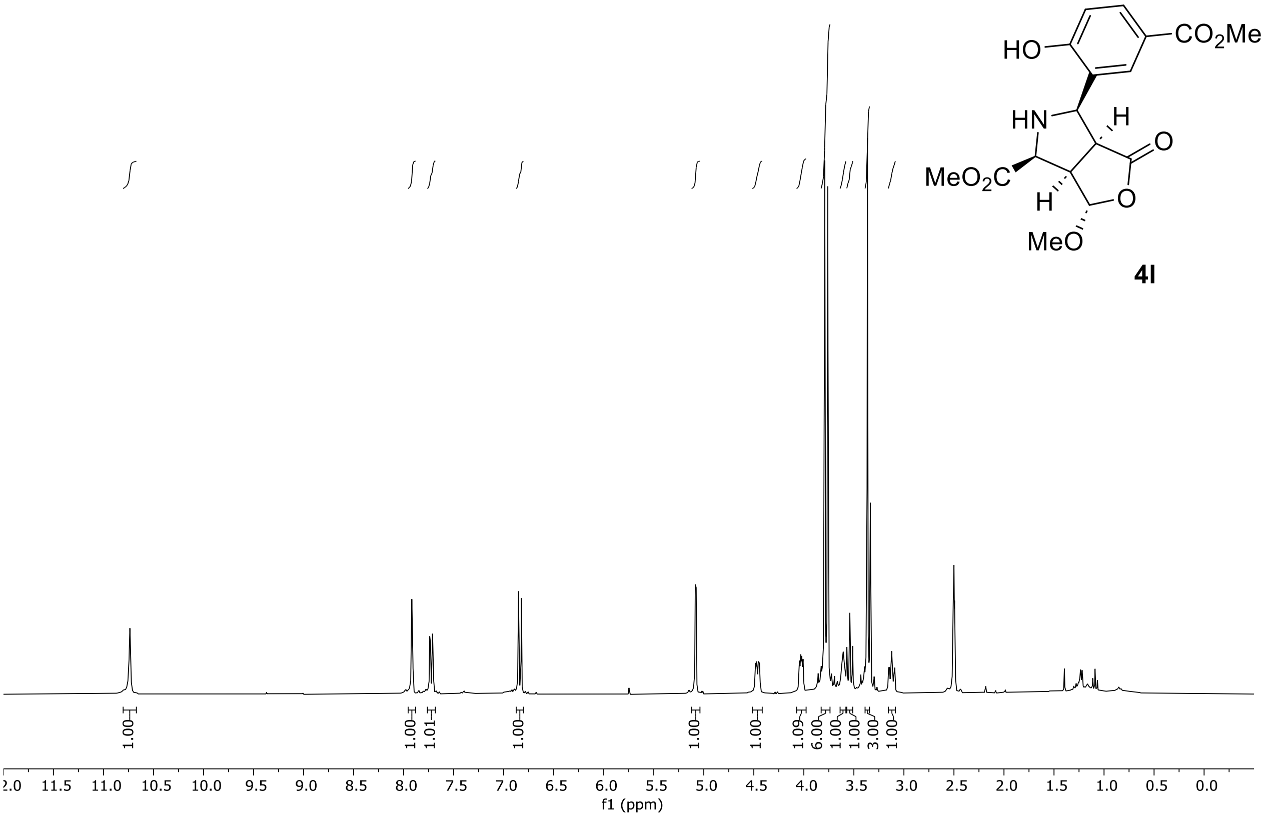


Figure S51. ^{13}H NMR spectrum (300 MHz, 298K, $(CD_3)_2SO$) of **4l**.

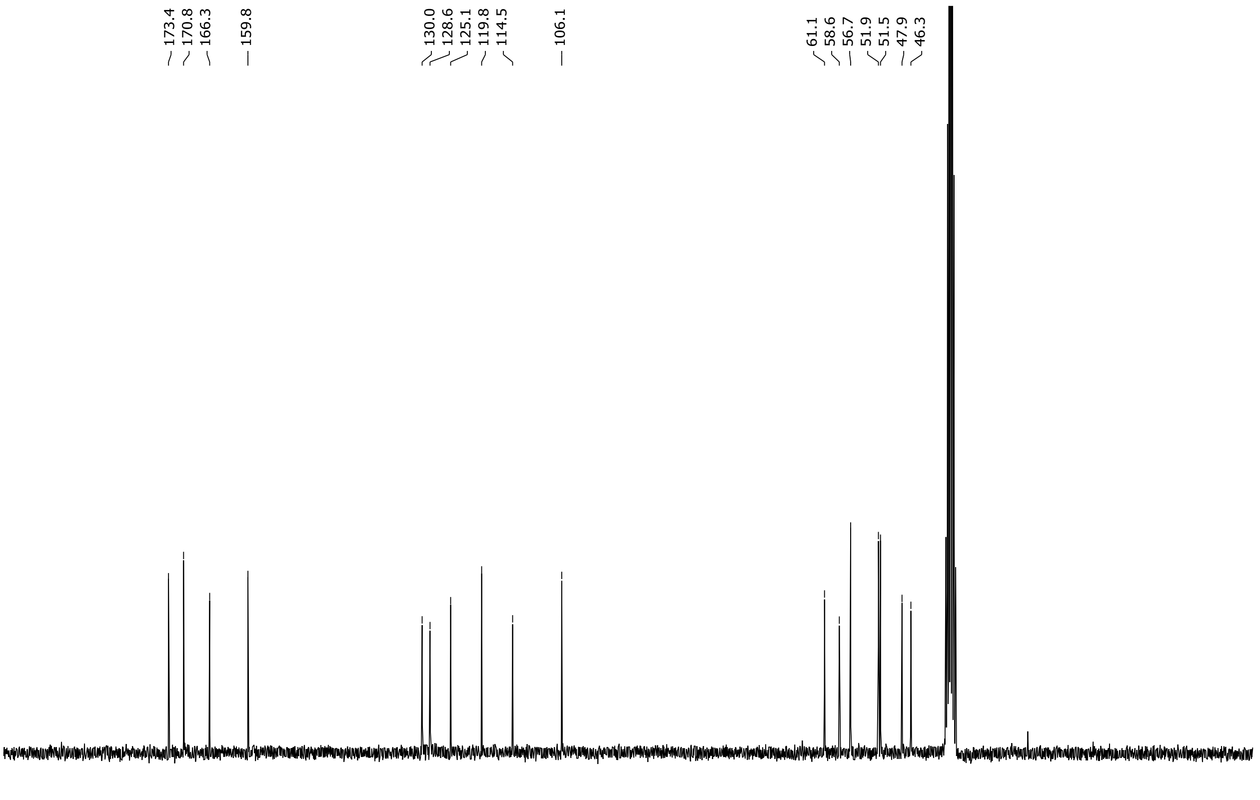


Figure S52. ^{13}C NMR spectrum (75 MHz, 298K, $(CD_3)_2SO$) of **4l**.

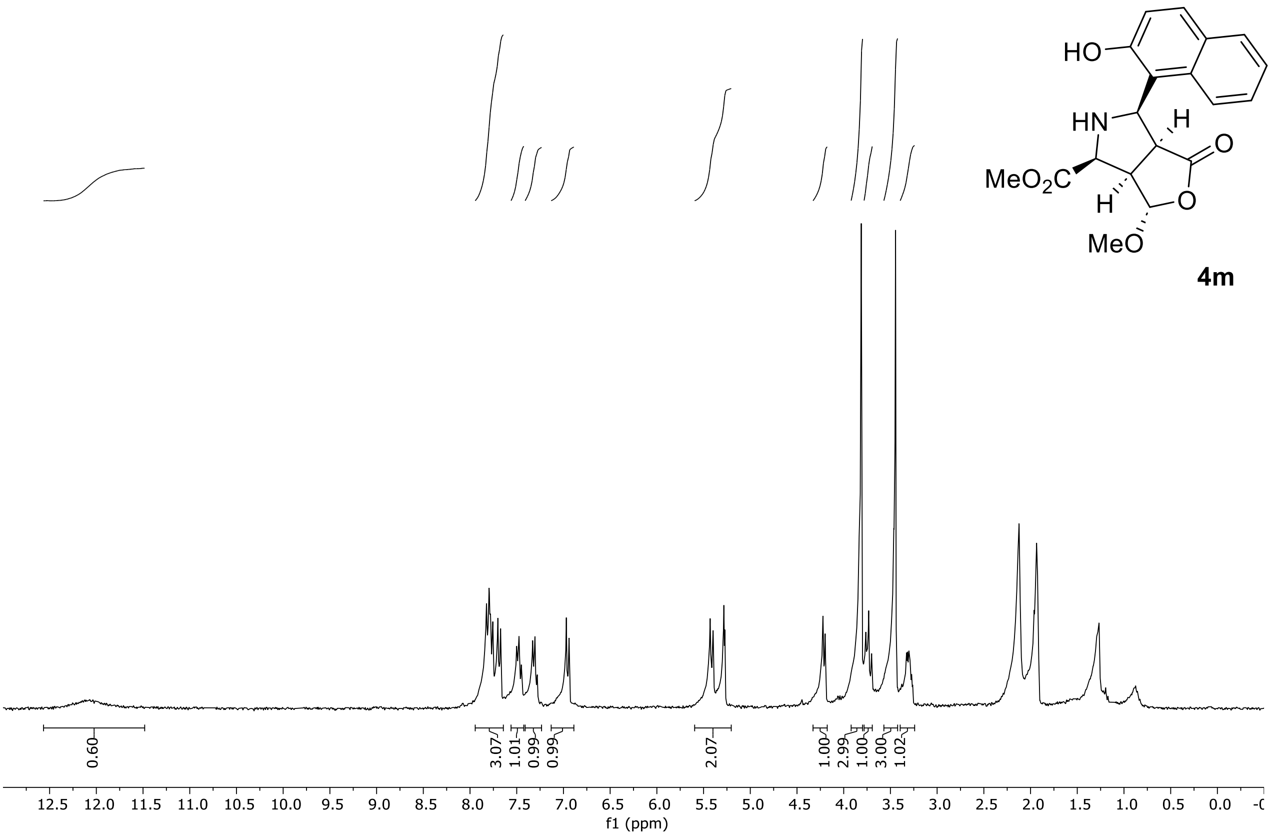


Figure S53. ^{1}H NMR spectrum (300 MHz, 298K, CD_3CN) of **4m**.

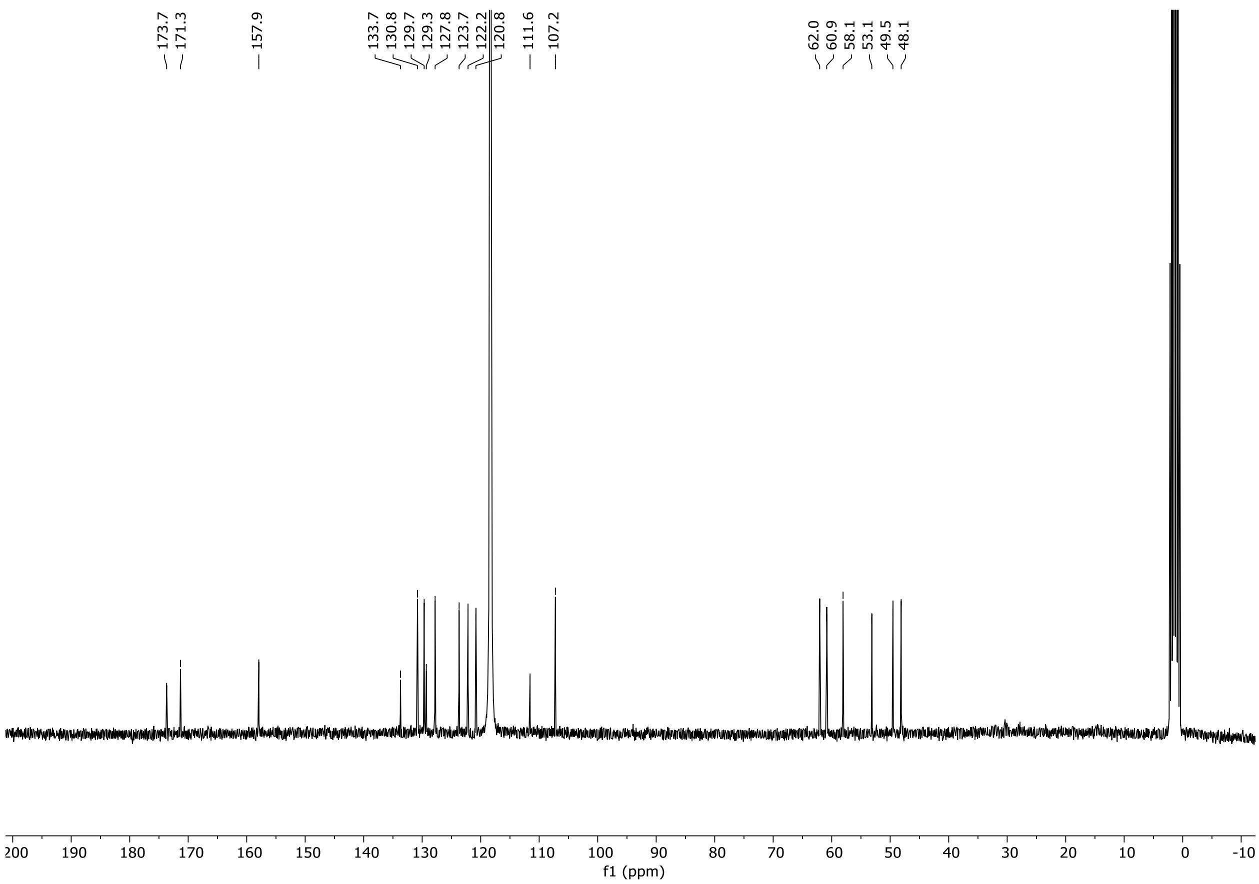


Figure S54. ^{13}C NMR spectrum (75 MHz, 298K, CD_3CN) of **4m**.

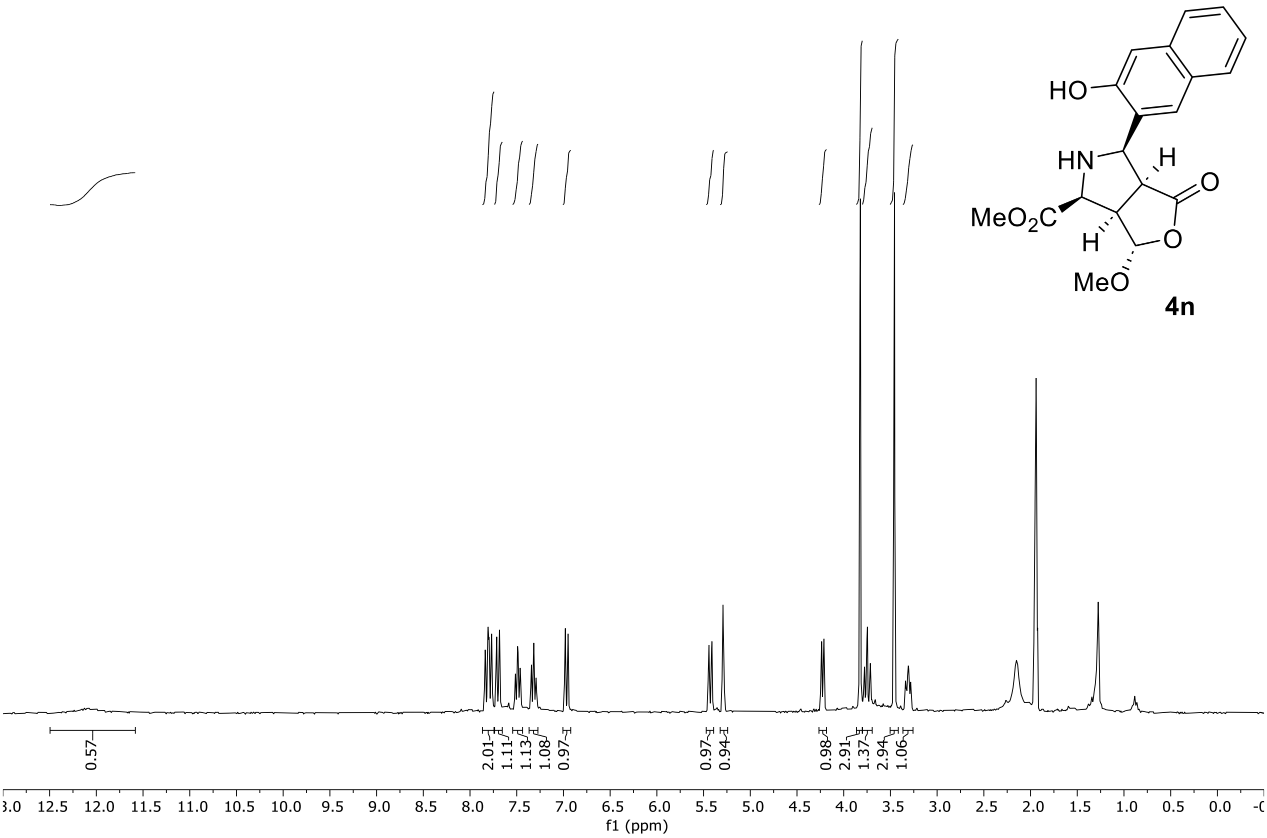


Figure S55. ^{1}H NMR spectrum (300 MHz, 298K, CD_3CN) of **4n**.

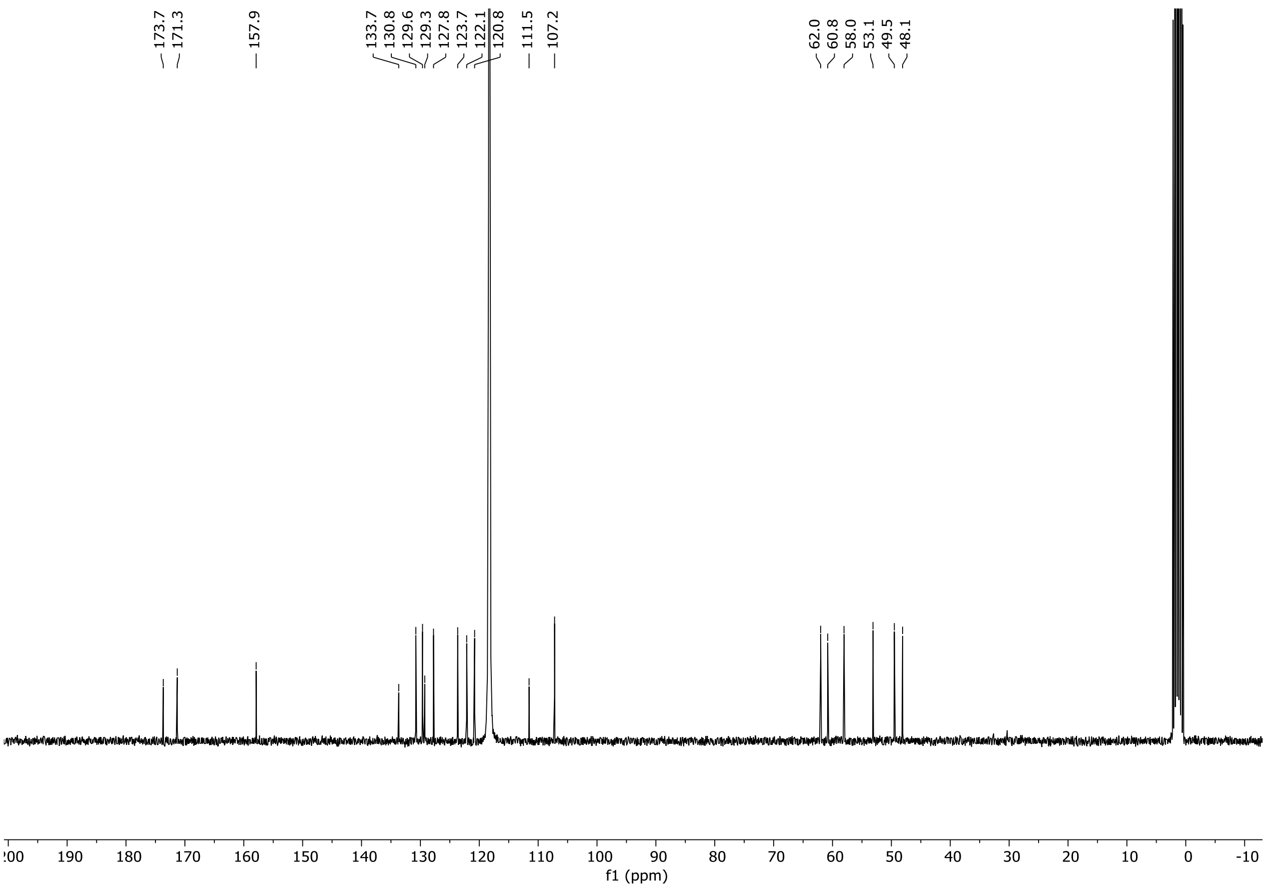
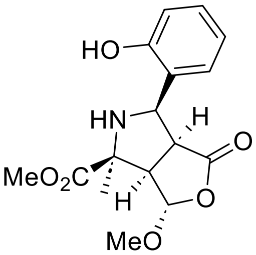


Figure S56. ^{13}C NMR spectrum (75 MHz, 298K, CD_3CN) of **4n**.



4o

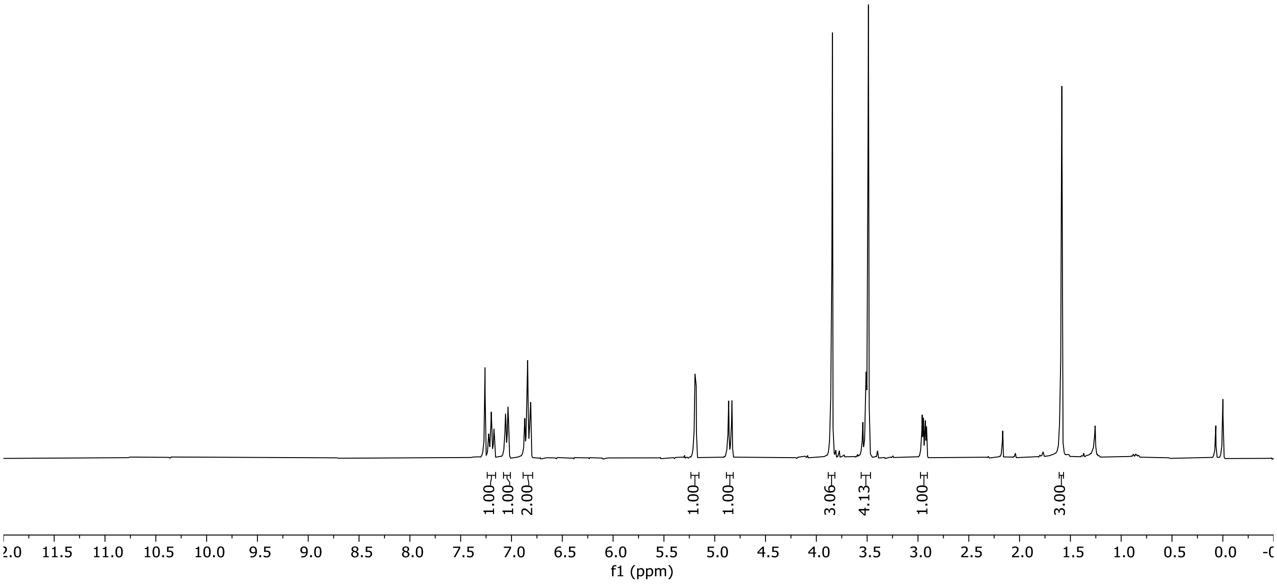


Figure S57. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **4o**.

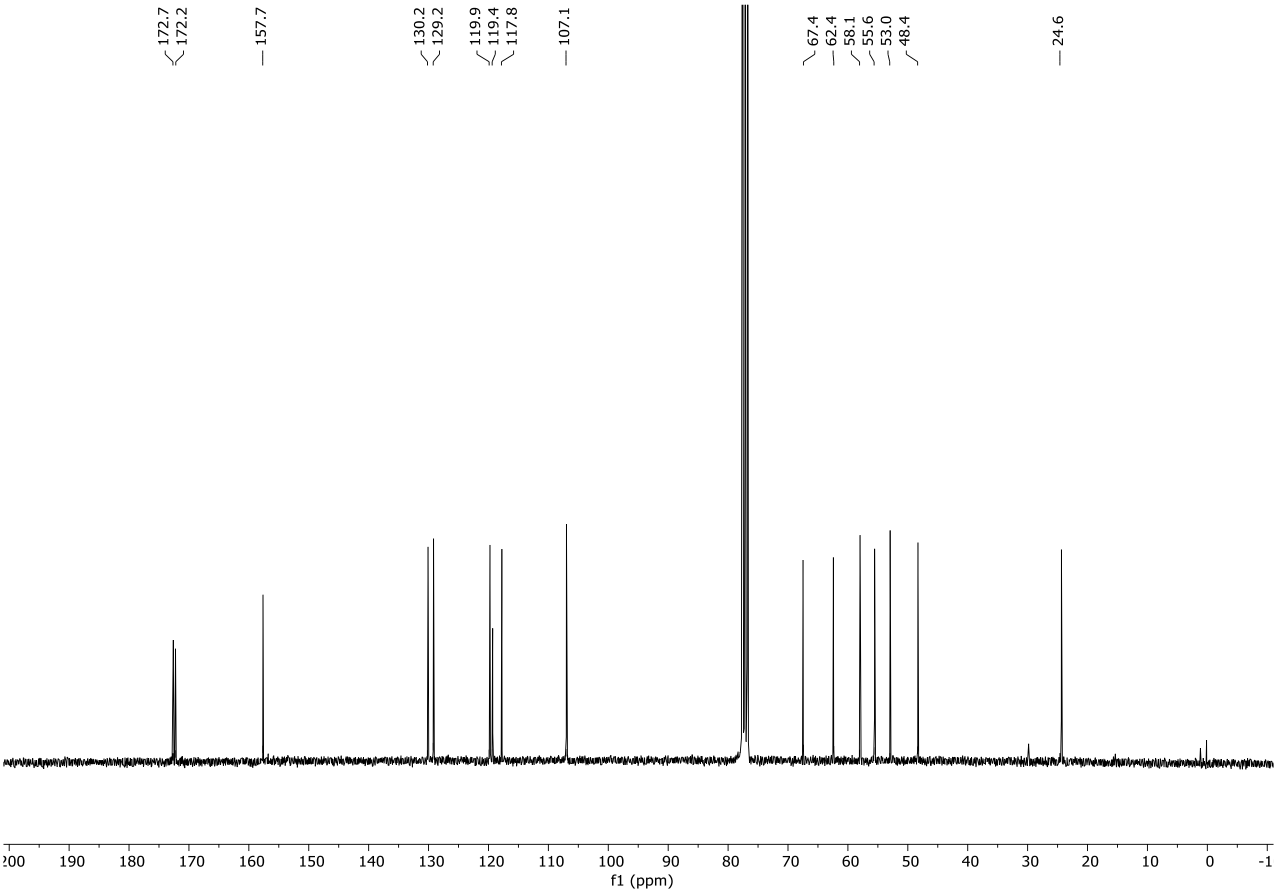


Figure S58. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **4o**.

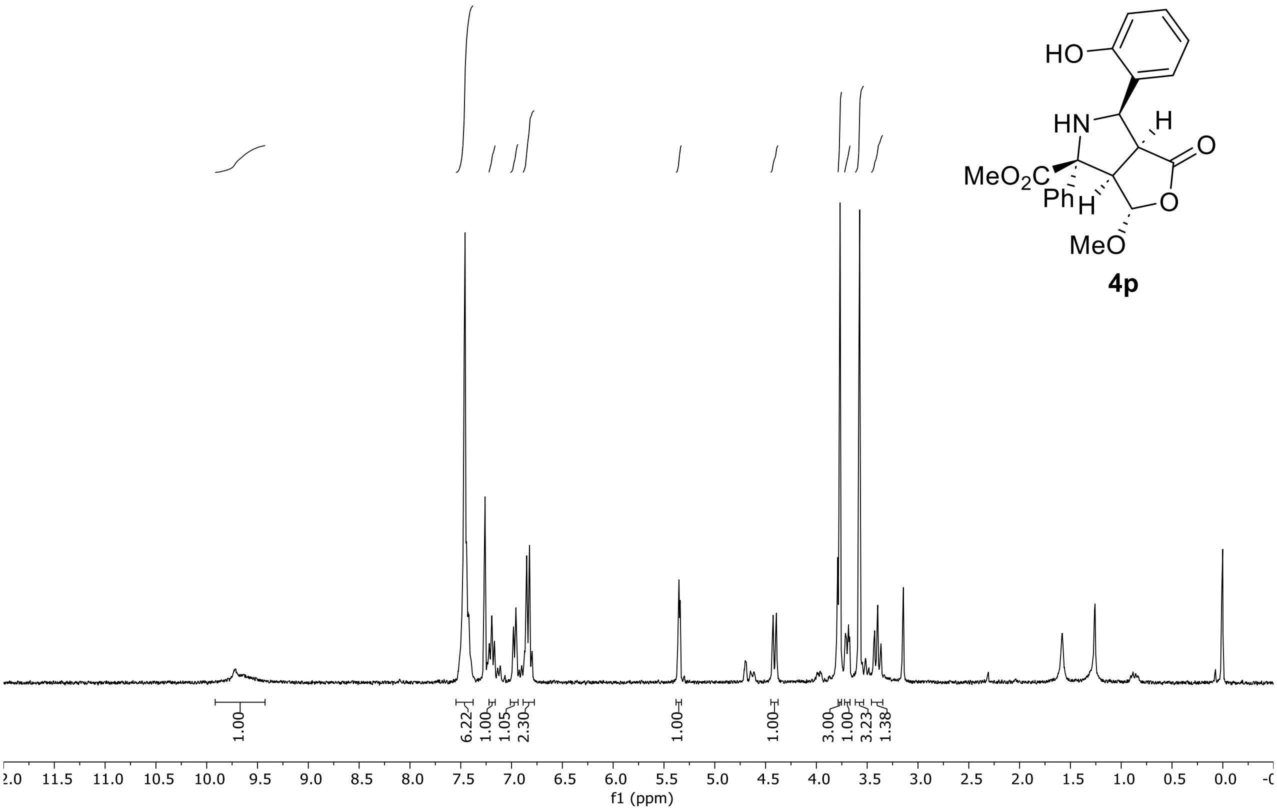


Figure S59. [1]H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **4p**. (d.r. = 5:1)

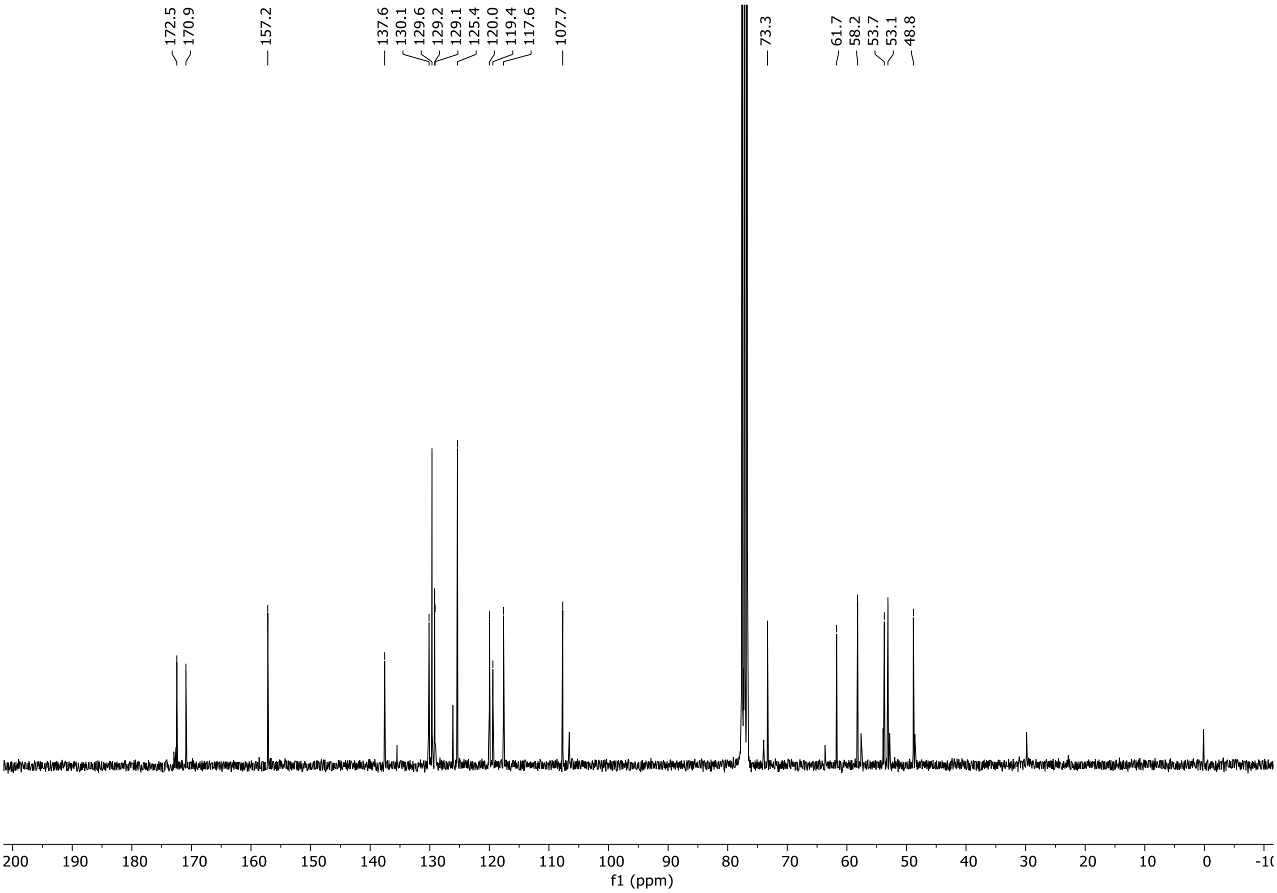


Figure S60. [13]C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **4p**. (d.r. = 5:1)

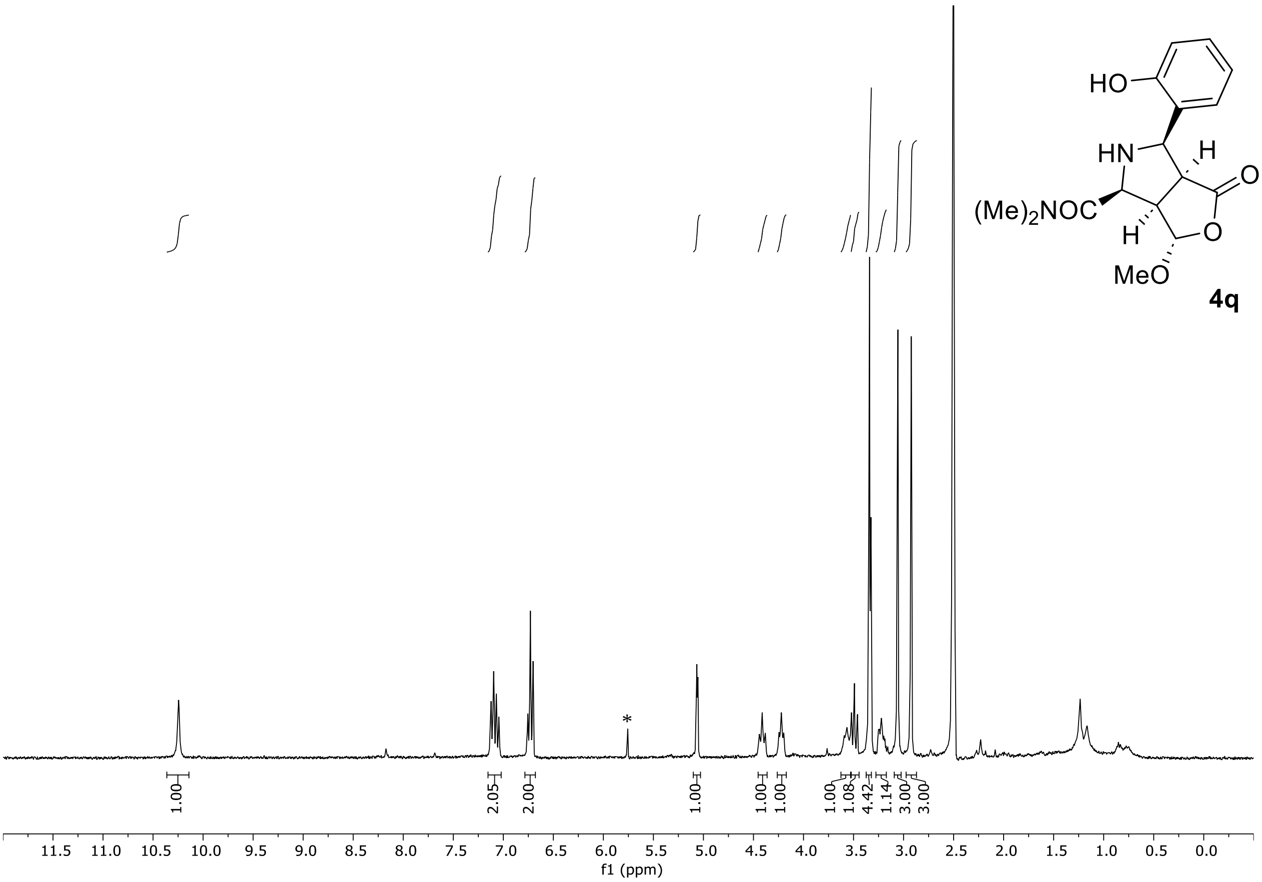


Figure S61. ^{1}H NMR spectrum (300 MHz, 298K, $(CD_3)_2SO$) of **4q** ($^{*}CH_2Cl_2$ solvent peak).

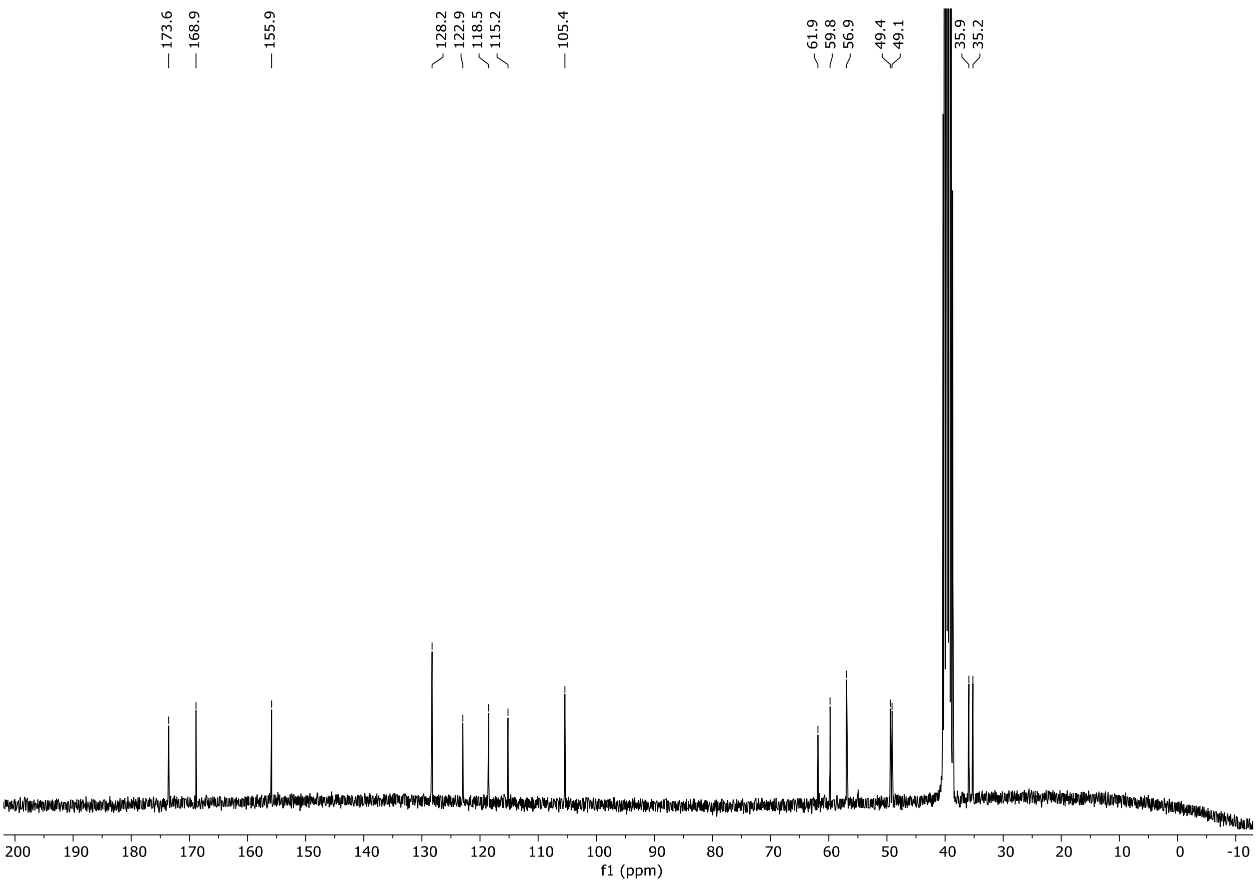


Figure S62. ^{13}C NMR spectrum (75 MHz, 298K, $(CD_3)_2SO$) of **4q**.

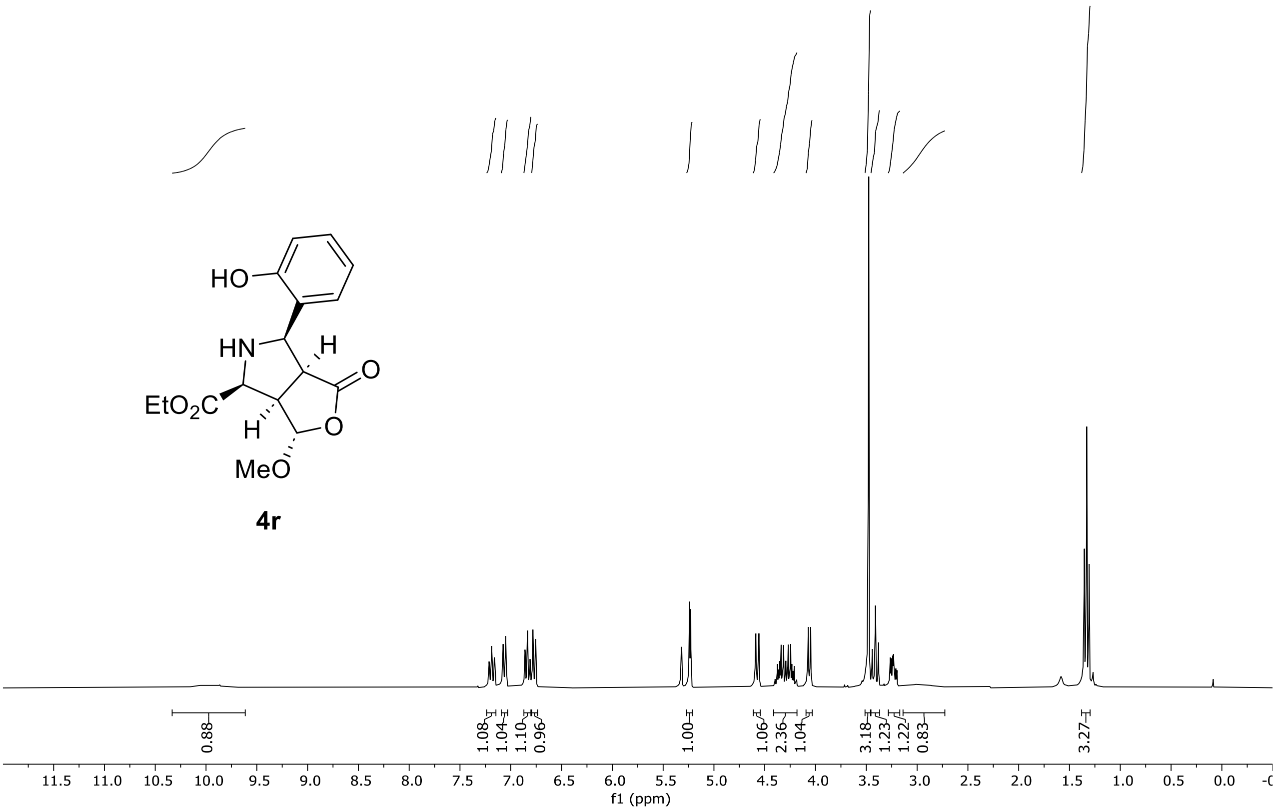


Figure S63. ^{1}H NMR spectrum (300 MHz, 298K, CD_2Cl_2) of **4r**.

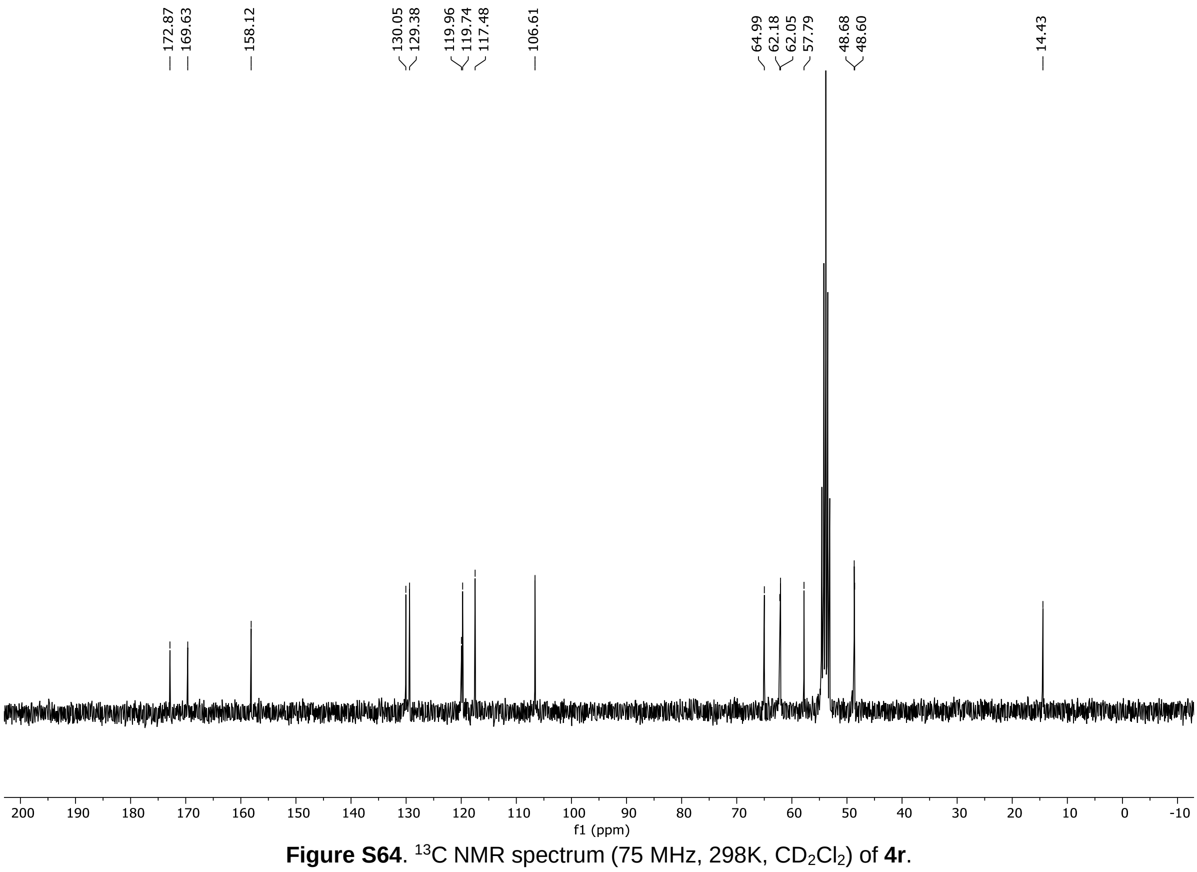


Figure S64. ^{13}C NMR spectrum (75 MHz, 298K, CD_2Cl_2) of **4r**.

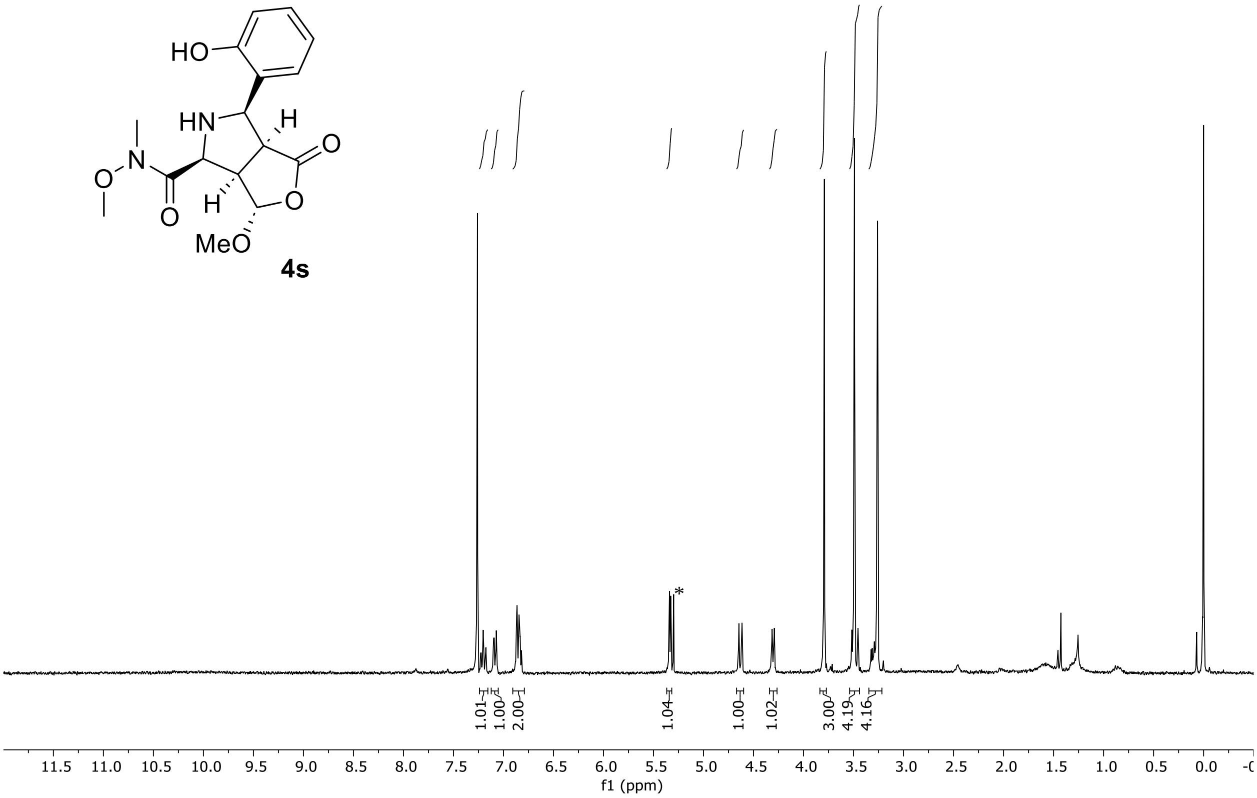


Figure S65. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **4s** ($^{*}CH_2Cl_2$ solvent peak).

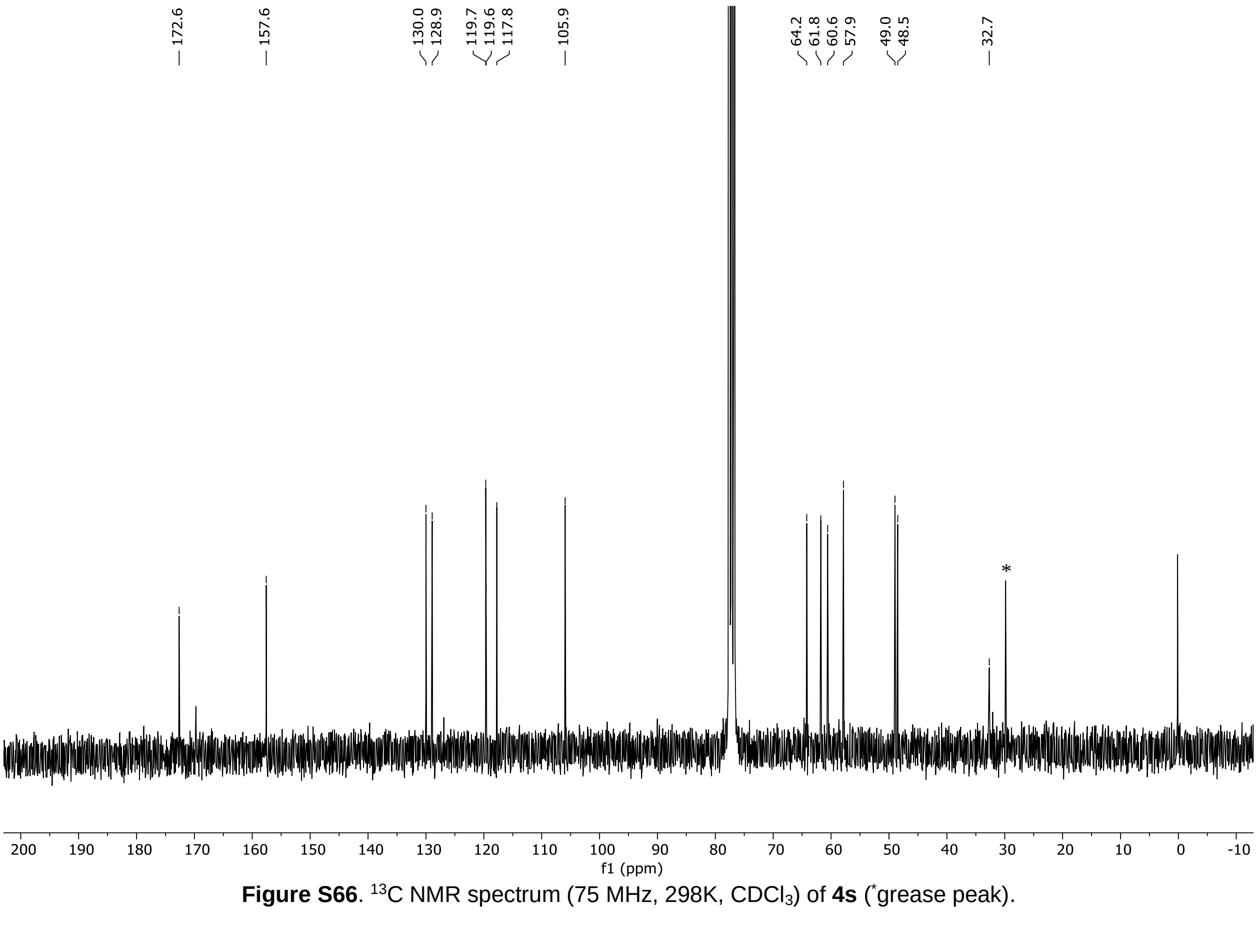


Figure S66. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **4s** (*grease peak).

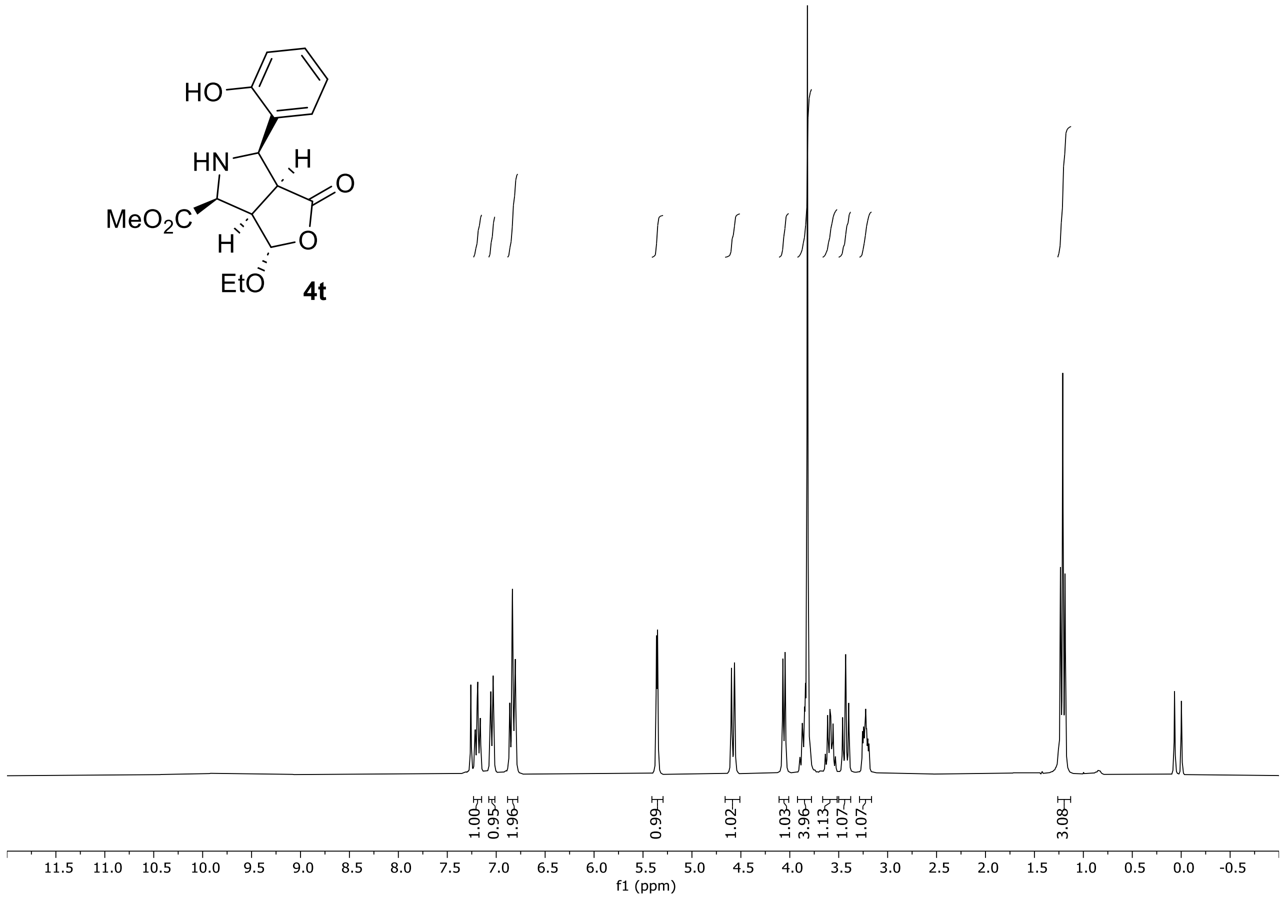


Figure S67. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **4t**.

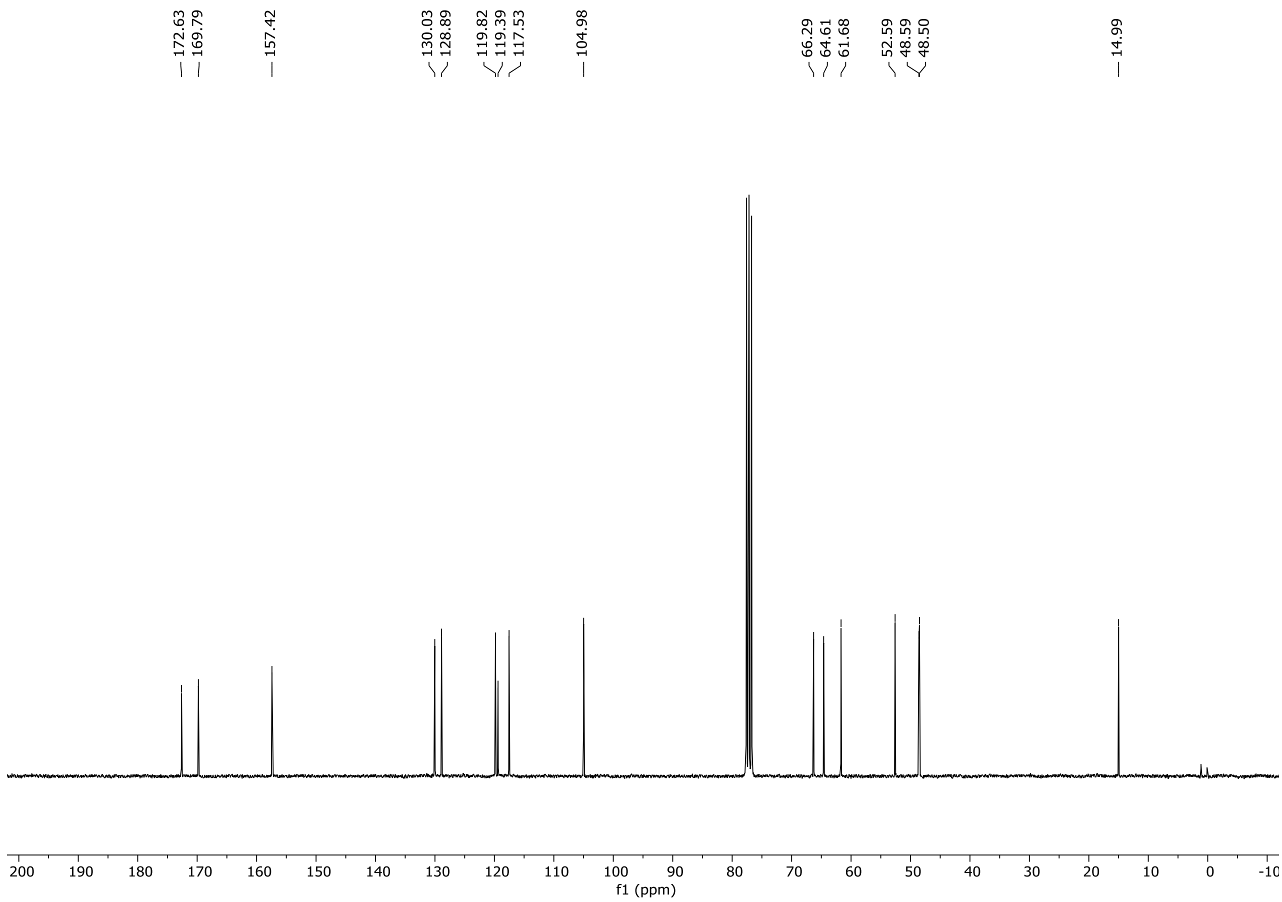


Figure S68. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **4t**.

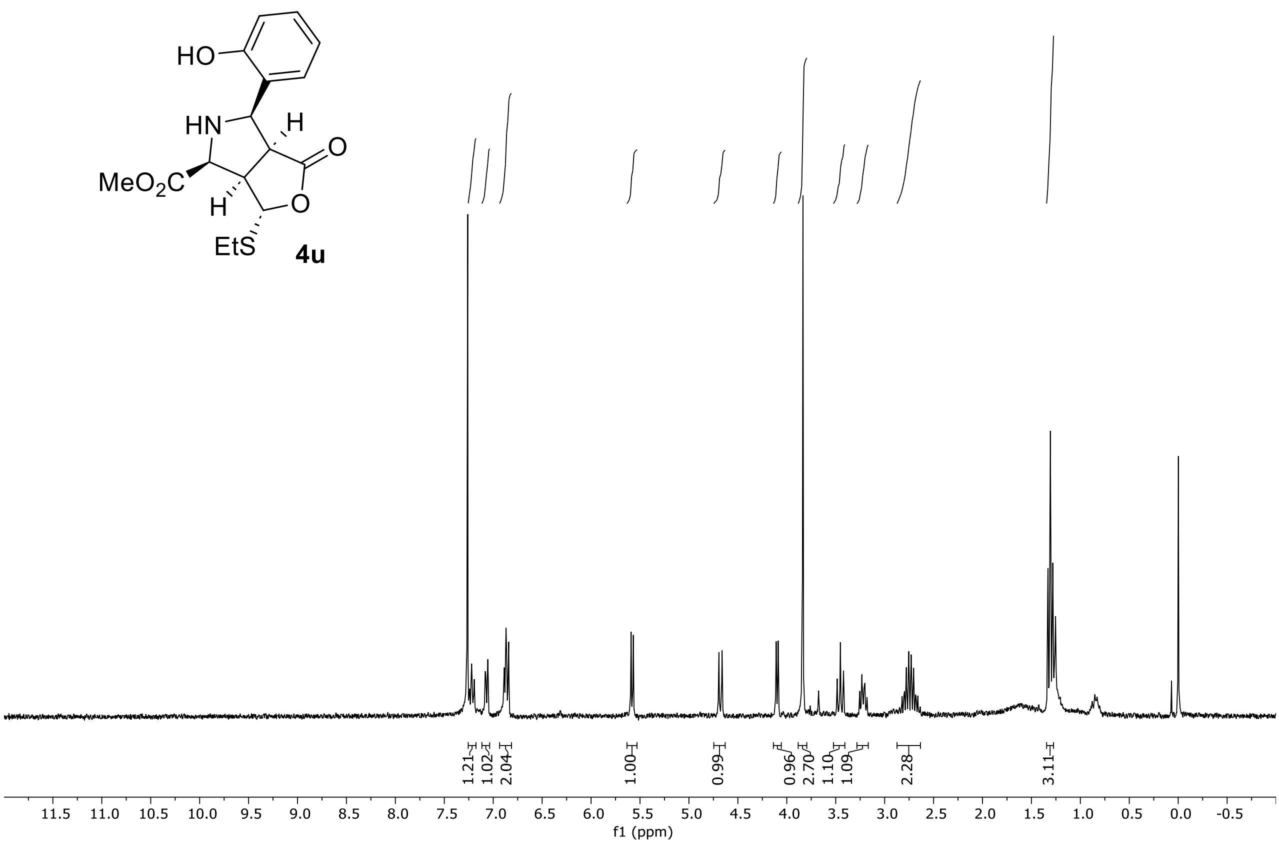


Figure S69. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **4u**.

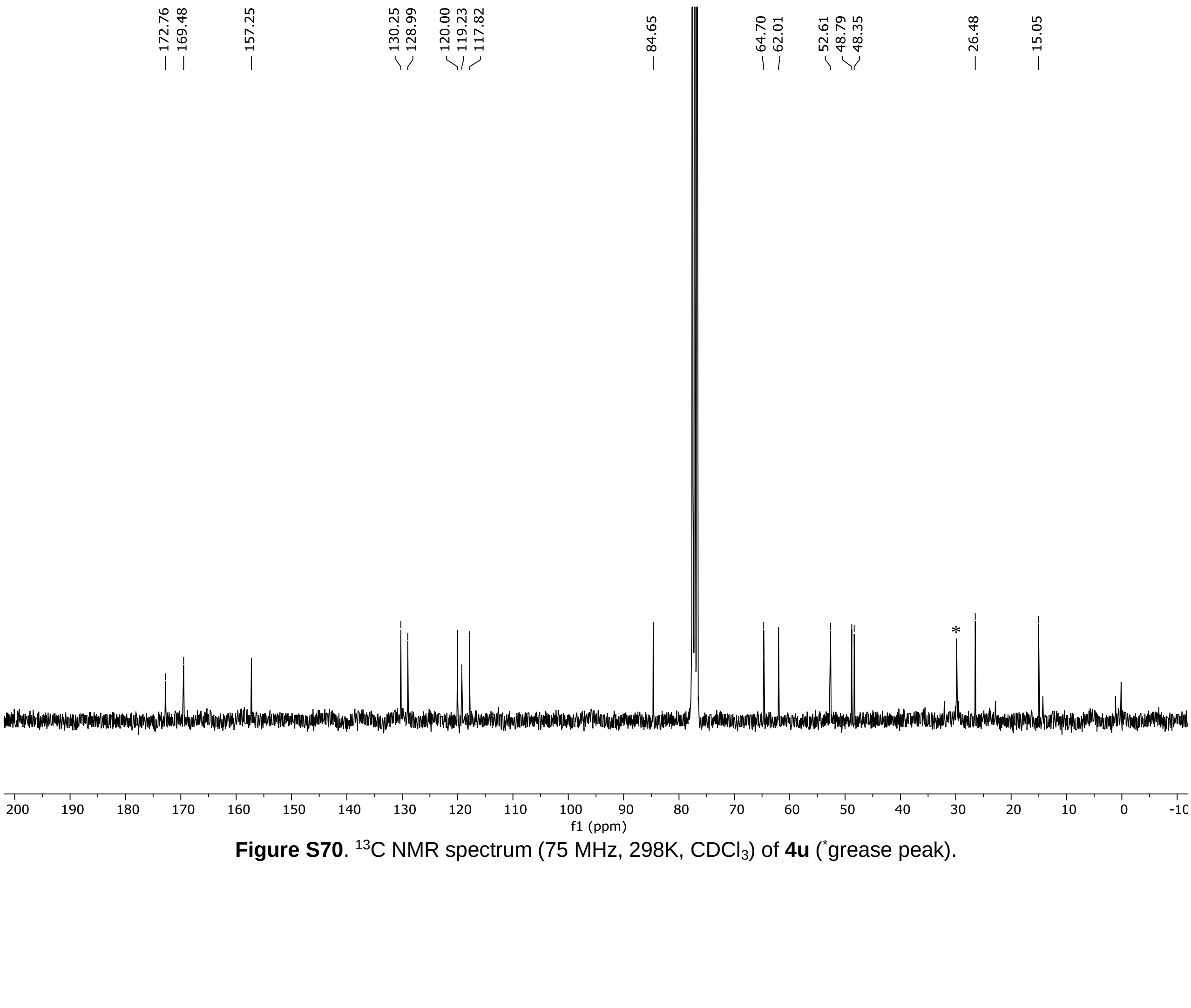


Figure S70. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **4u** (*grease peak).

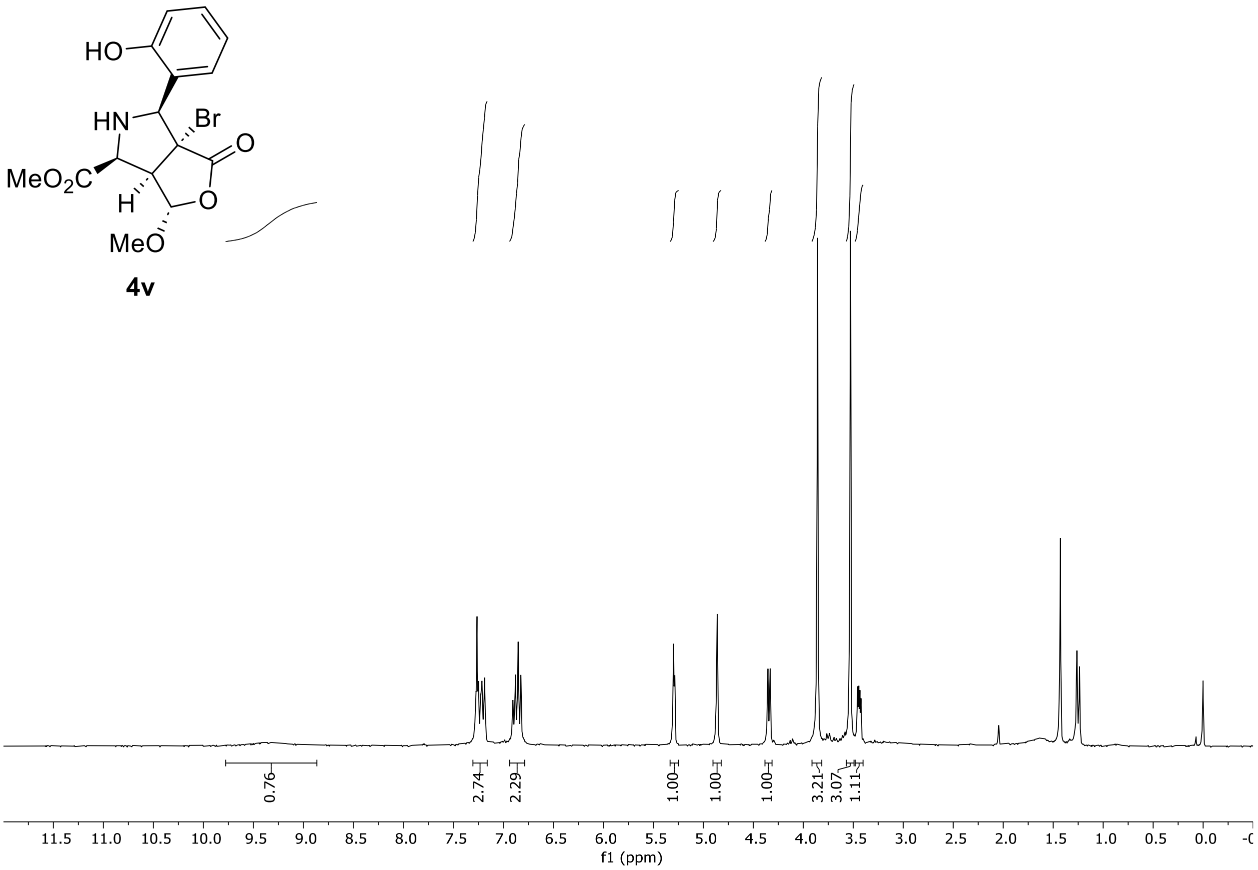


Figure S71. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **4v**.

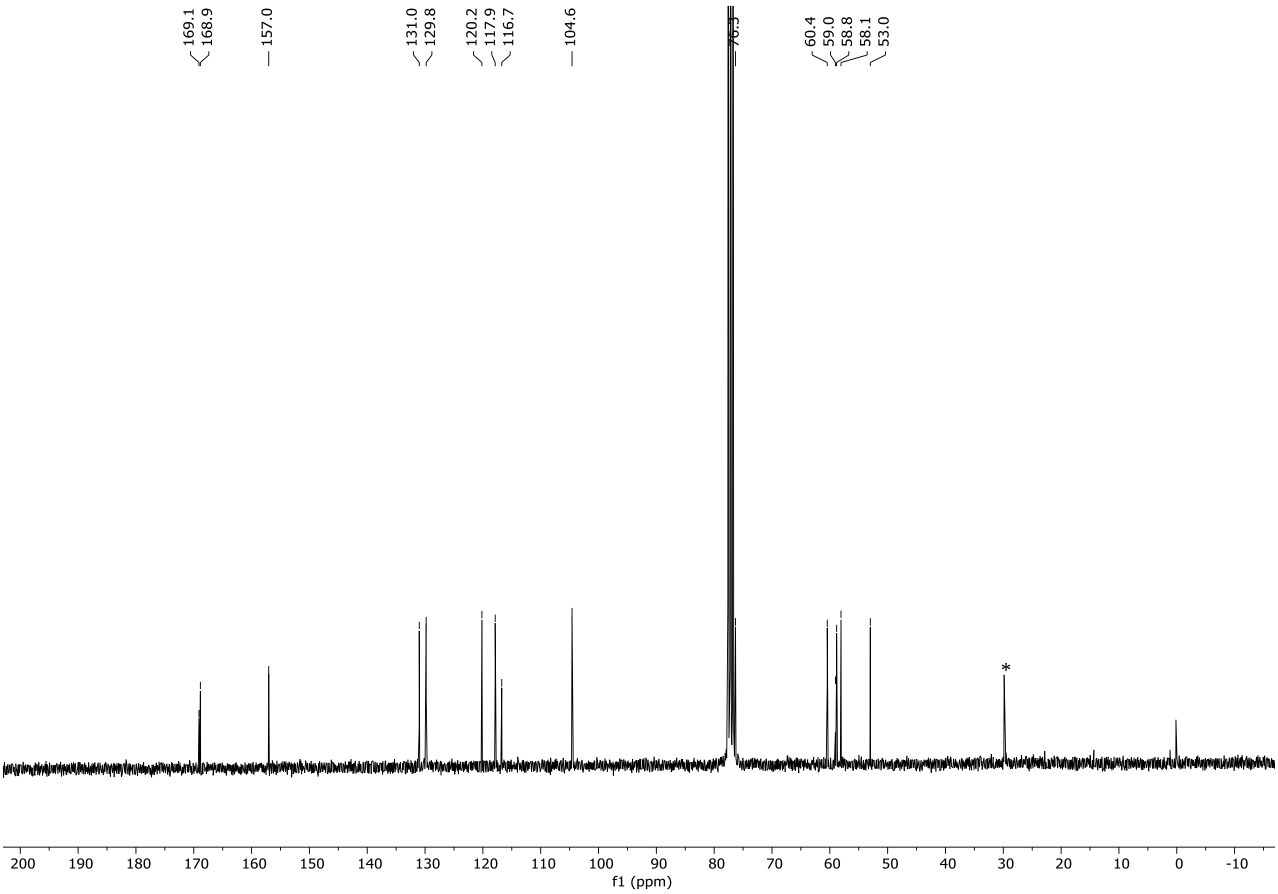


Figure S72. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **4v** (*grease peak).

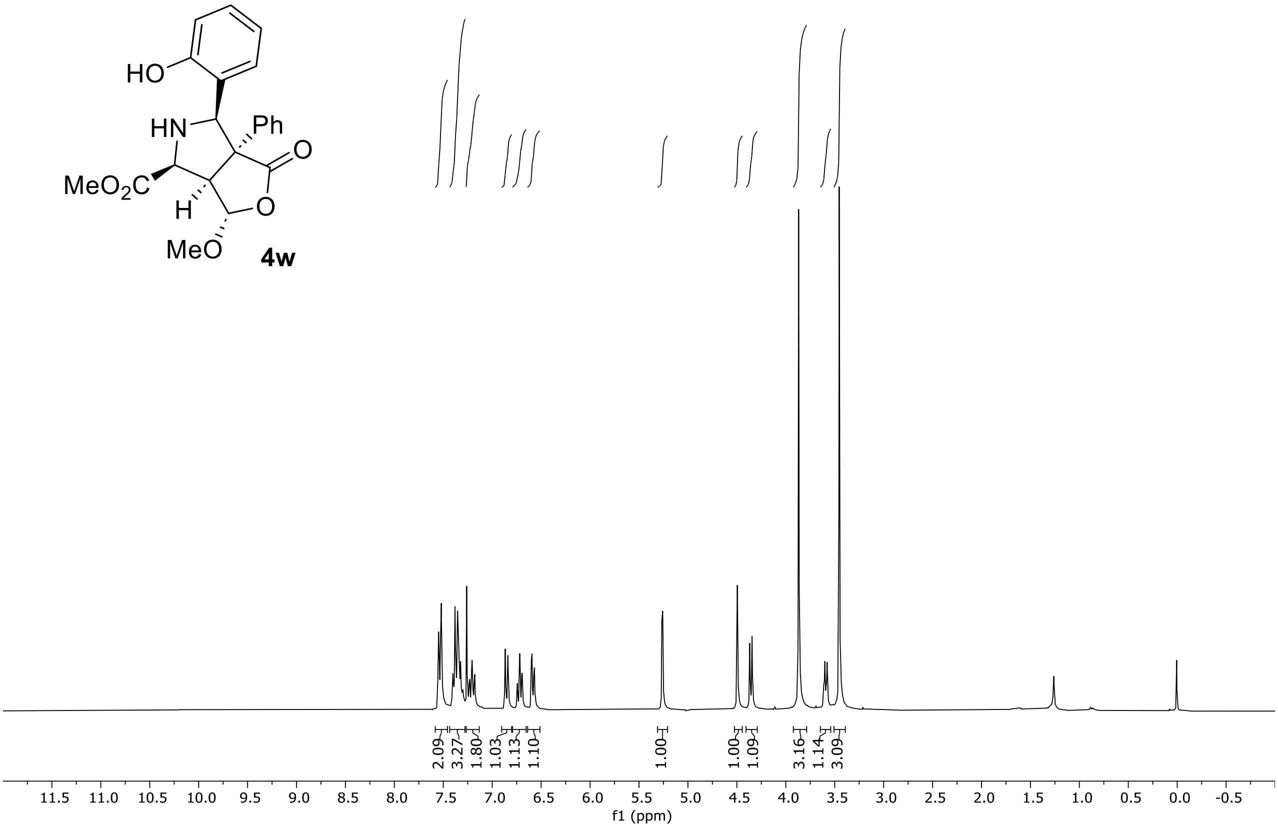


Figure S73. [1]H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **4w**.

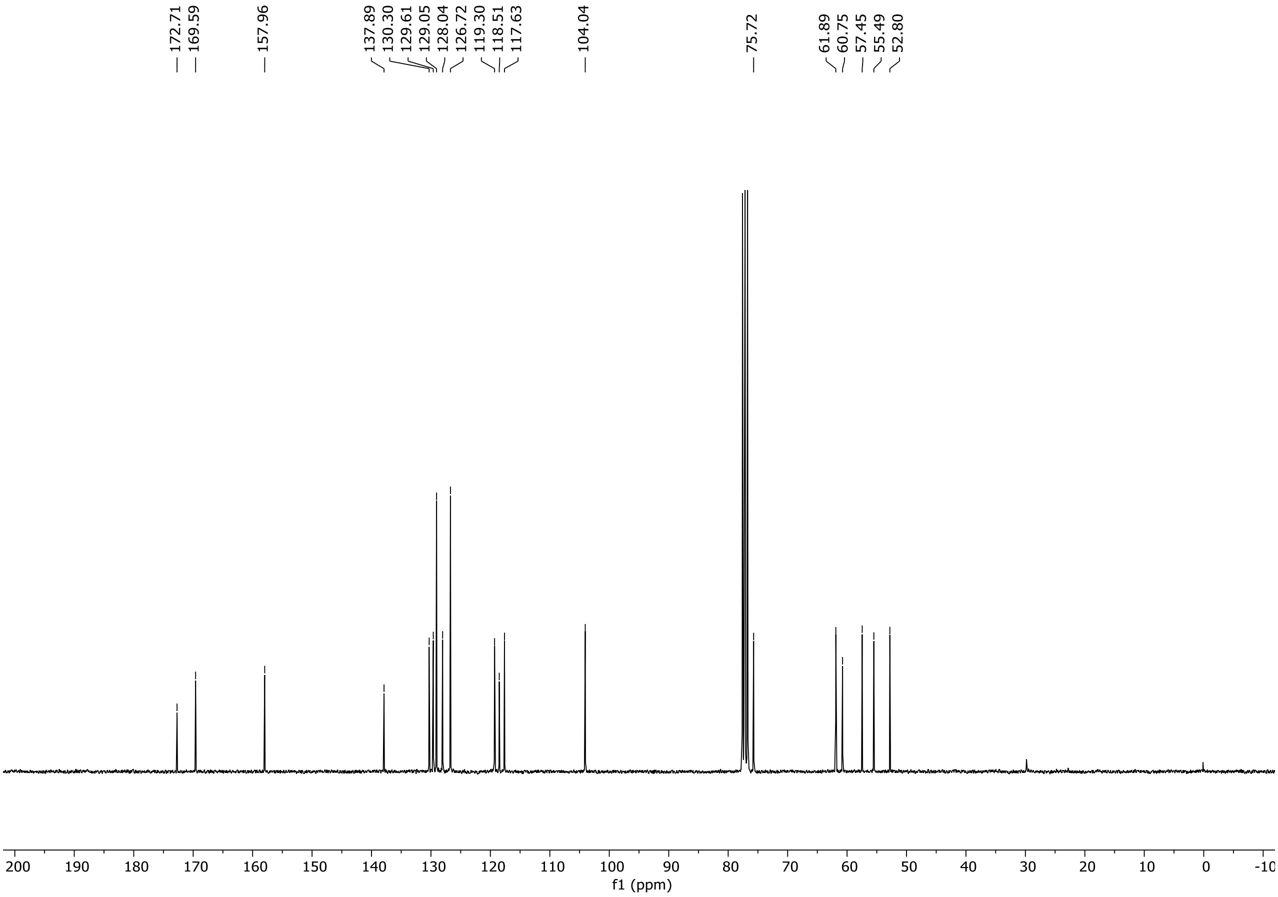


Figure S74. [13]C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **4w**.

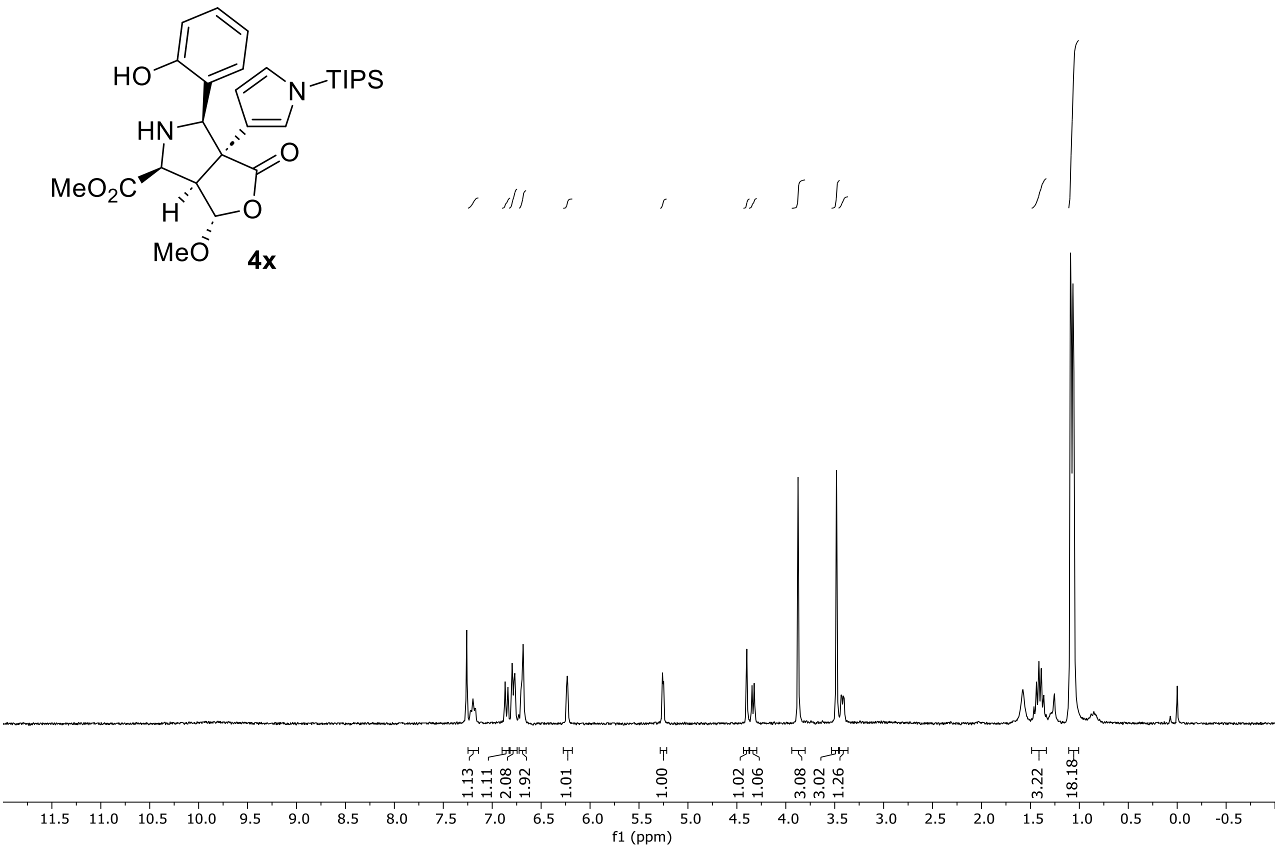


Figure S75. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **4x**.

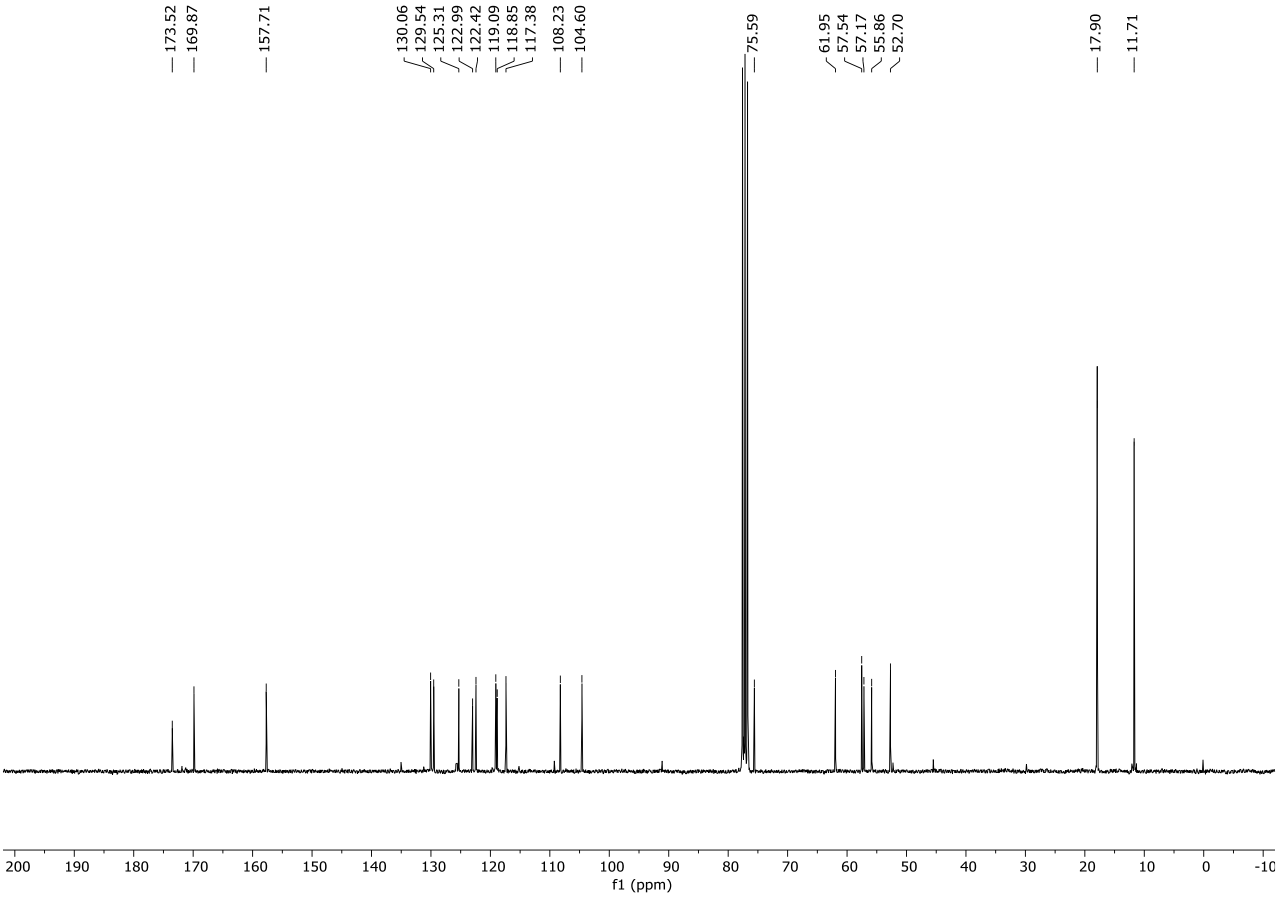
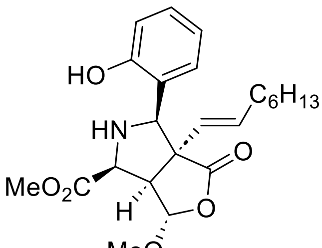


Figure S76. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **4x**.



4y

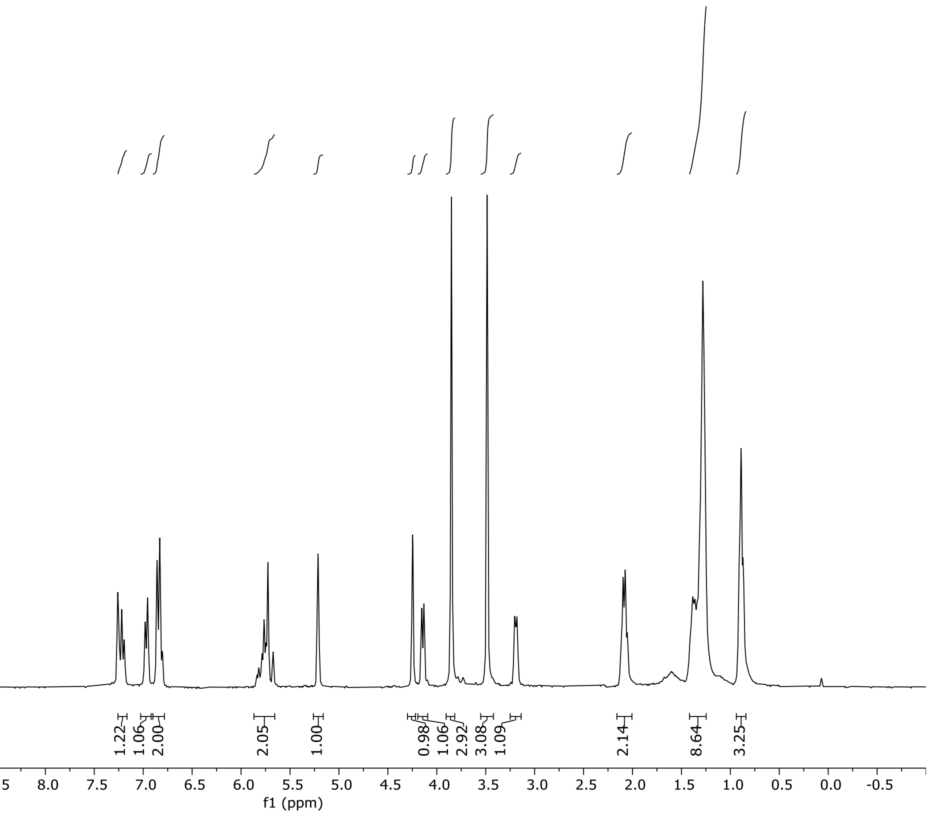


Figure S77. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **4y**.

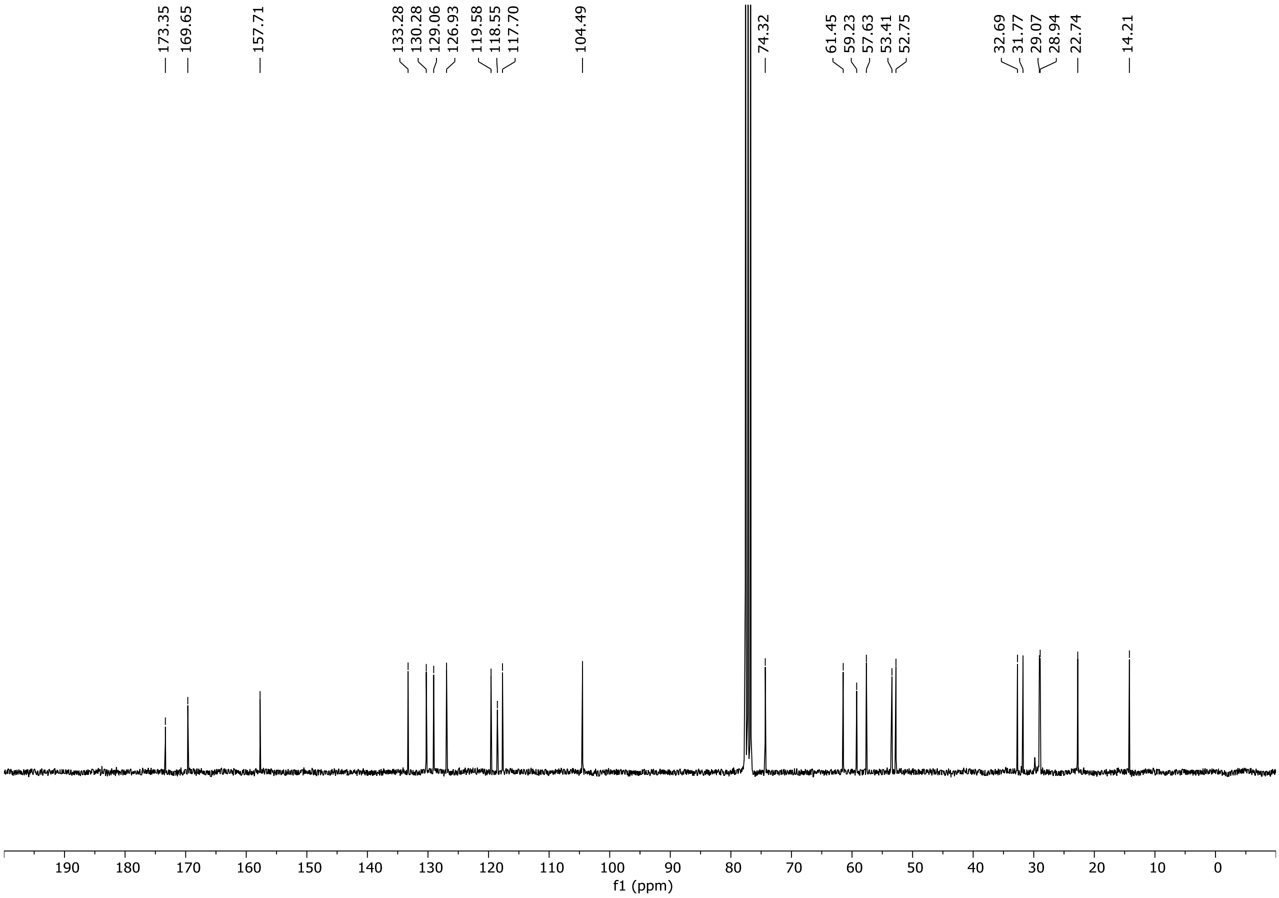


Figure S78. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **4y**.

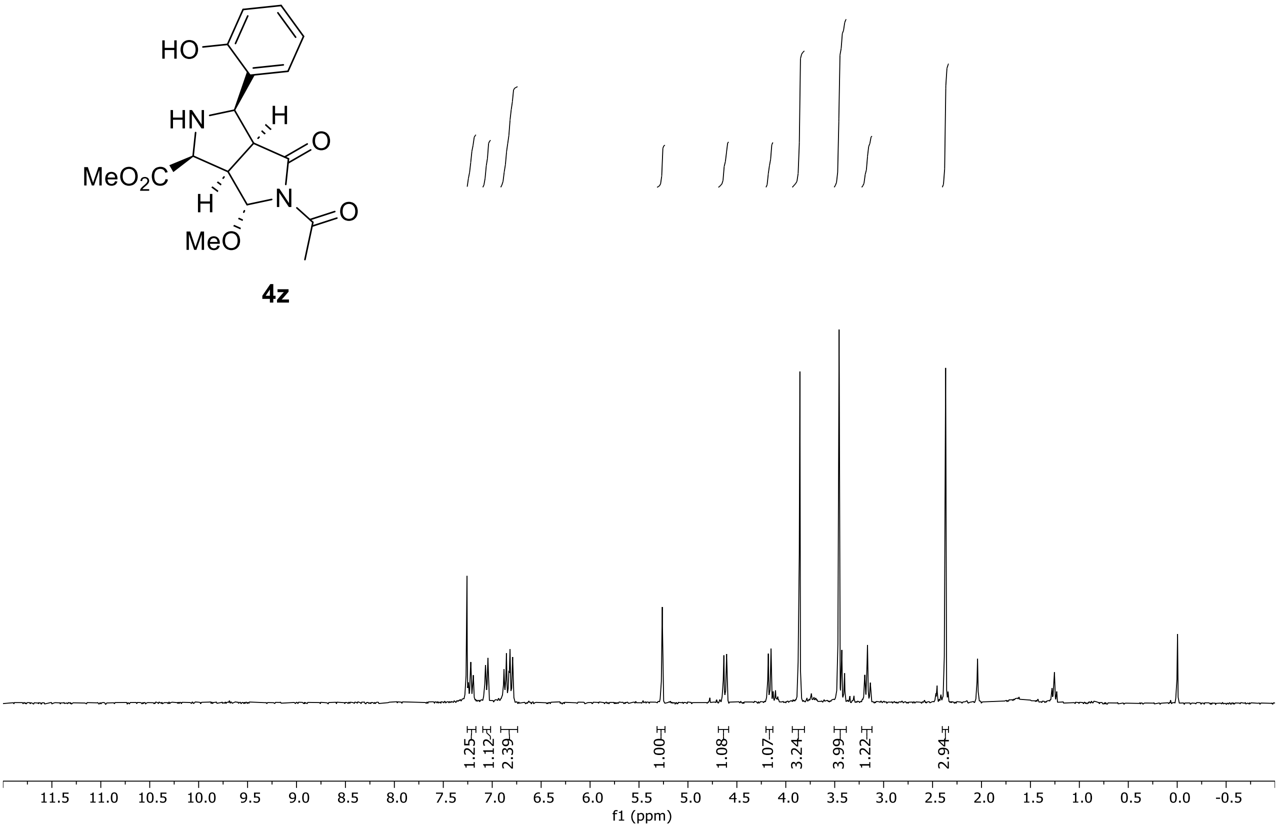


Figure S79. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **4z**.

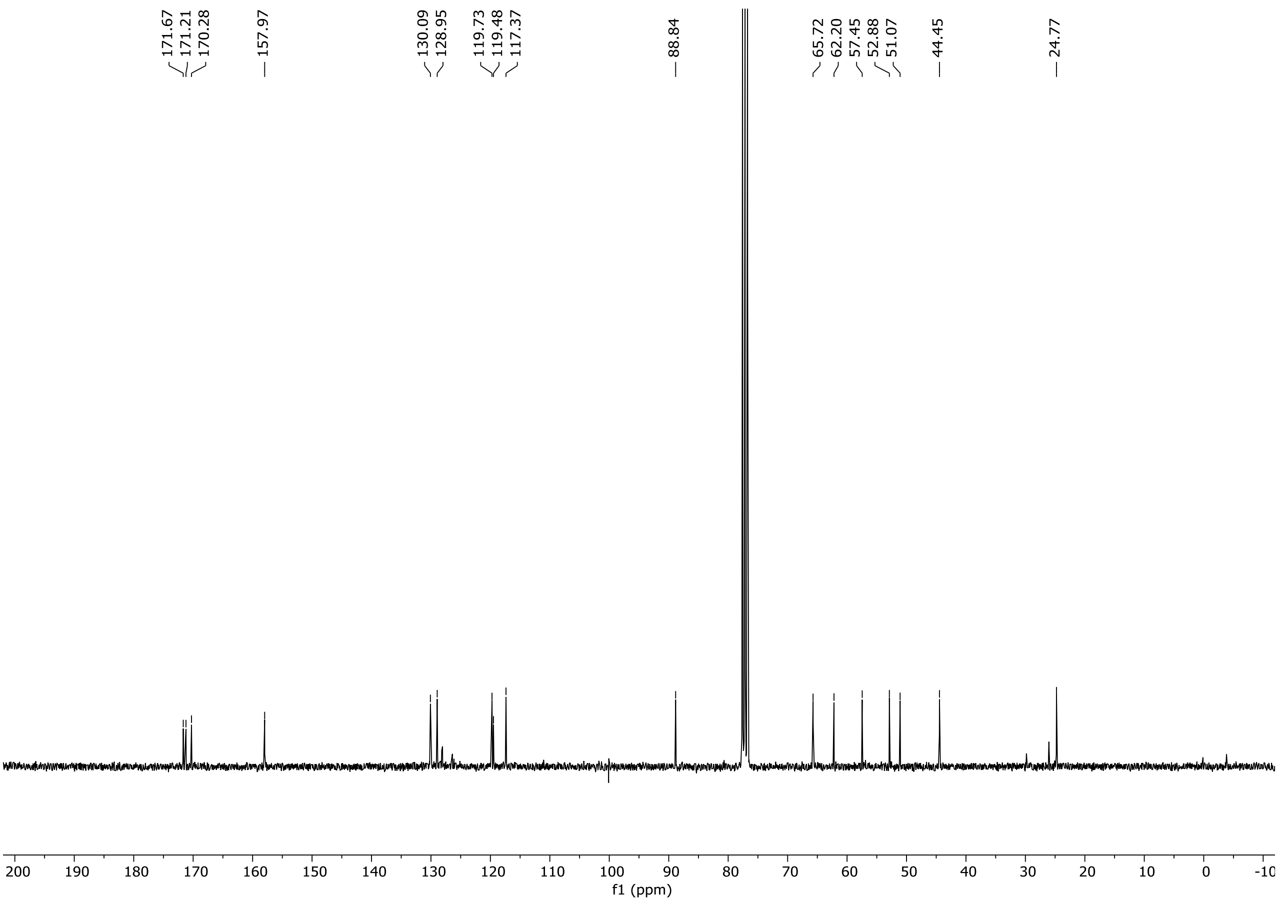


Figure S80. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **4z**.

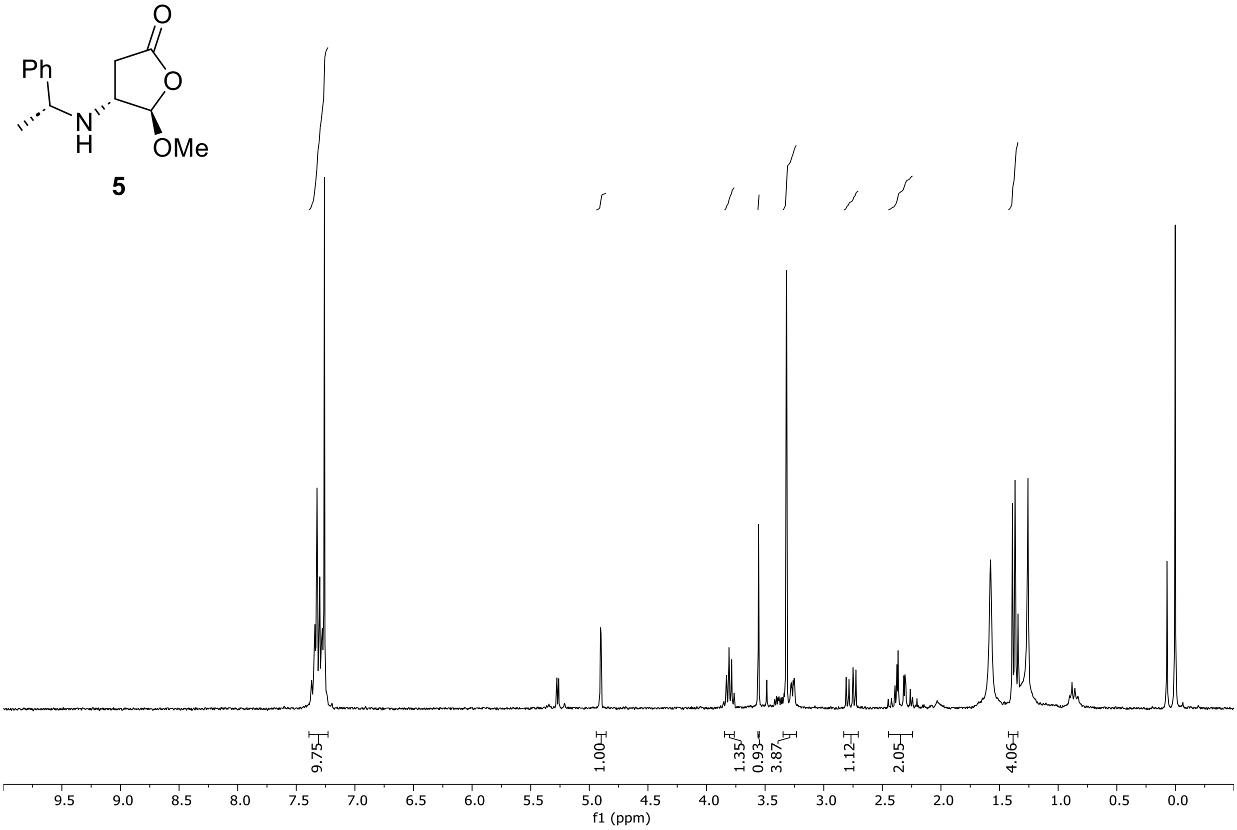


Figure S81. [1]H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **5**.

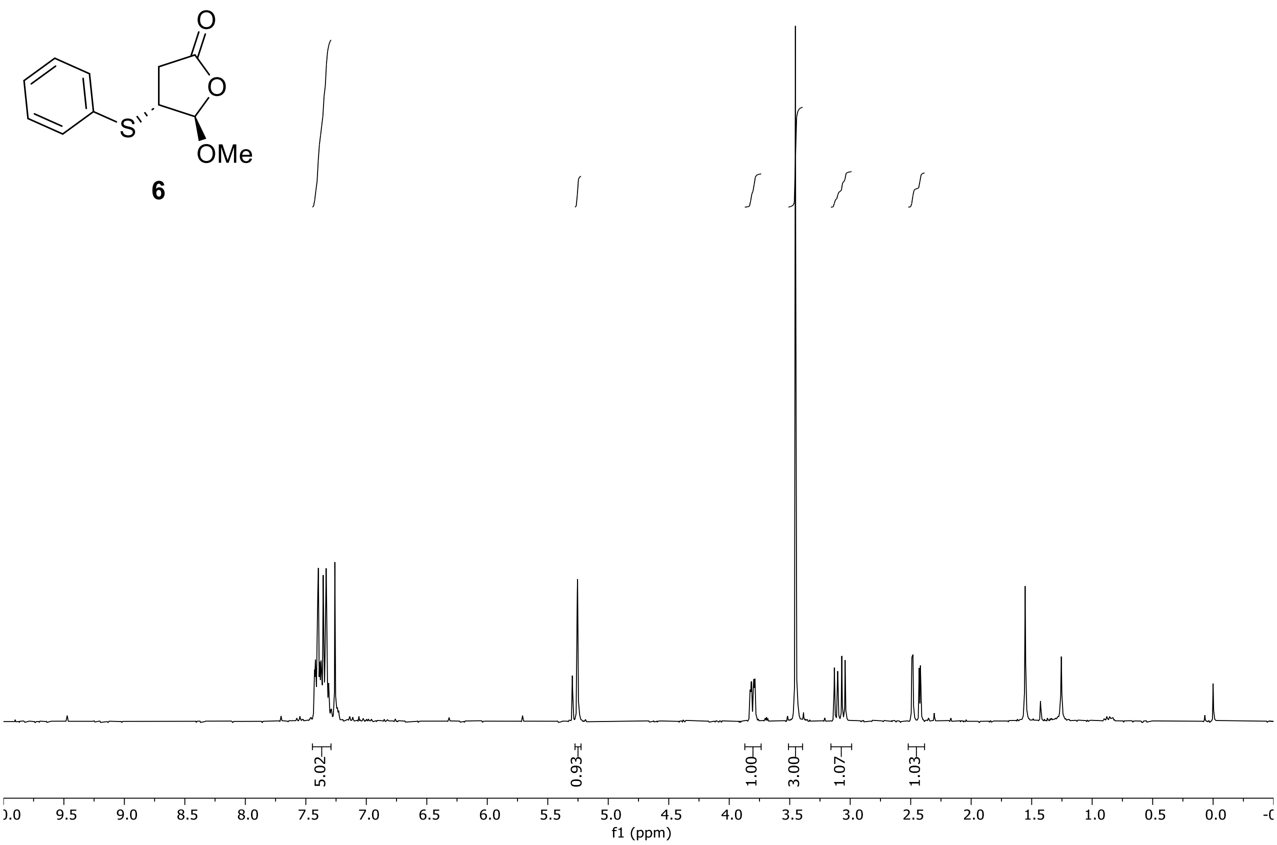


Figure S82. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **6**.

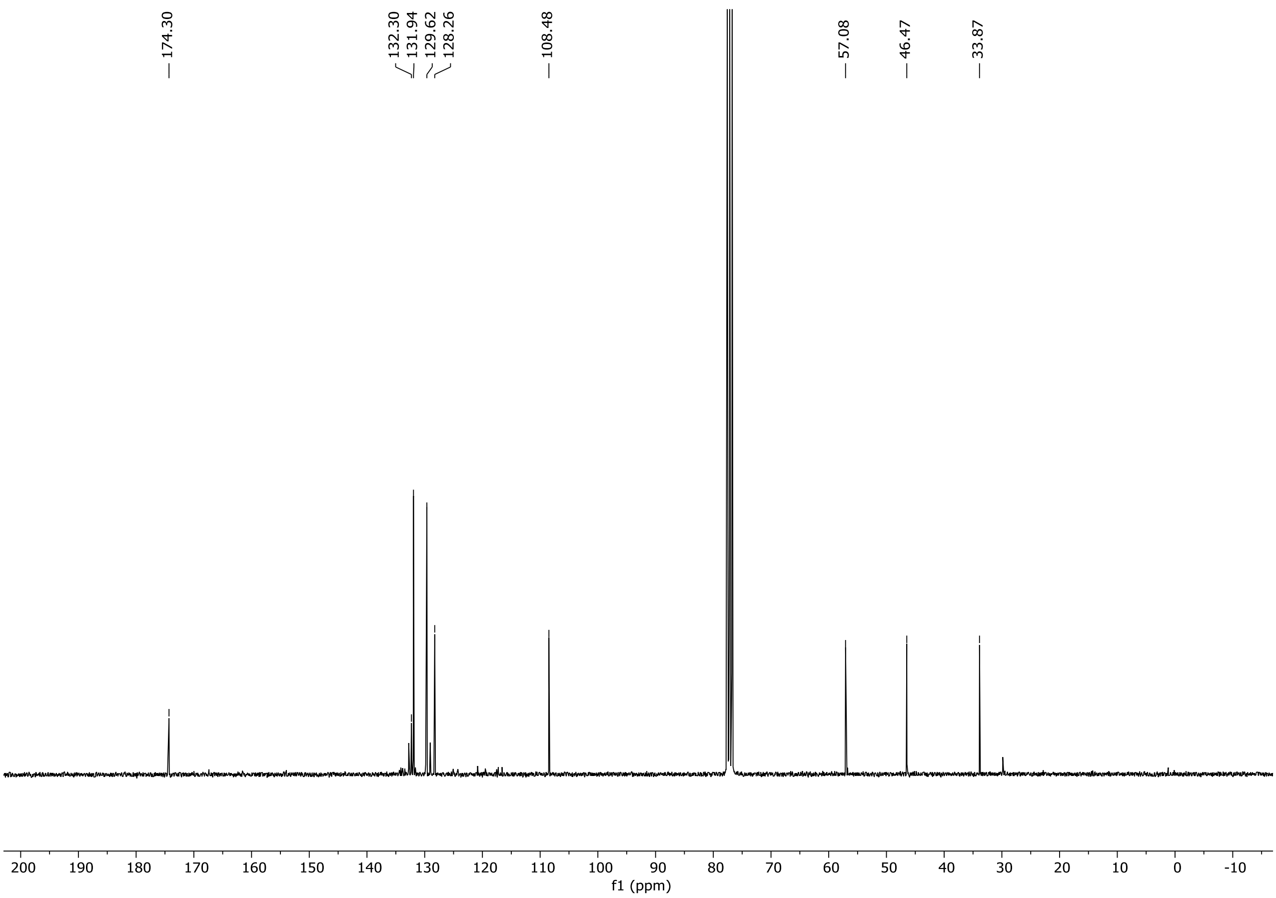
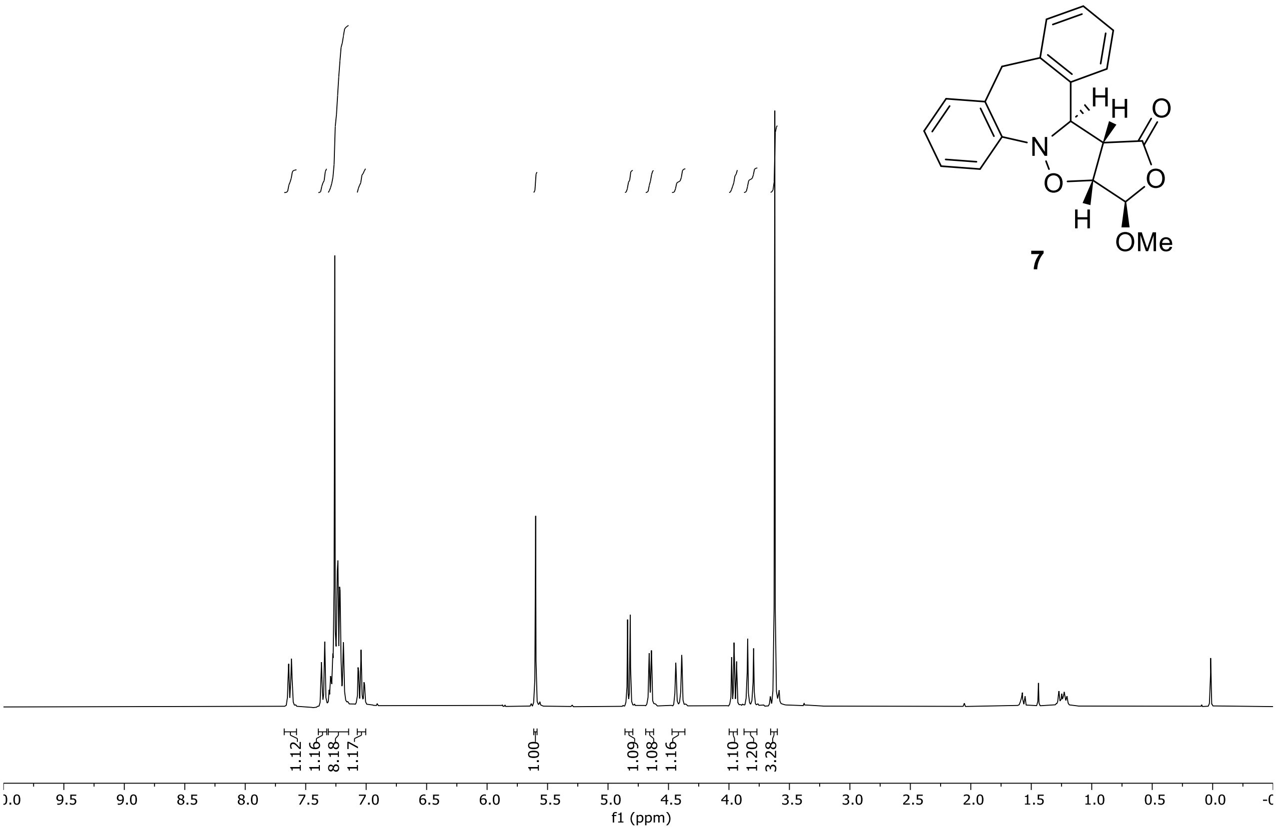


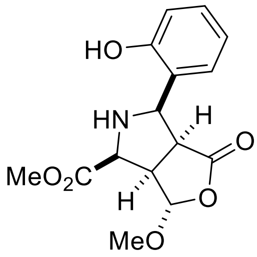
Figure S83. ^{13}C NMR spectrum (76 MHz, 298K, $CDCl_3$) of **6**.



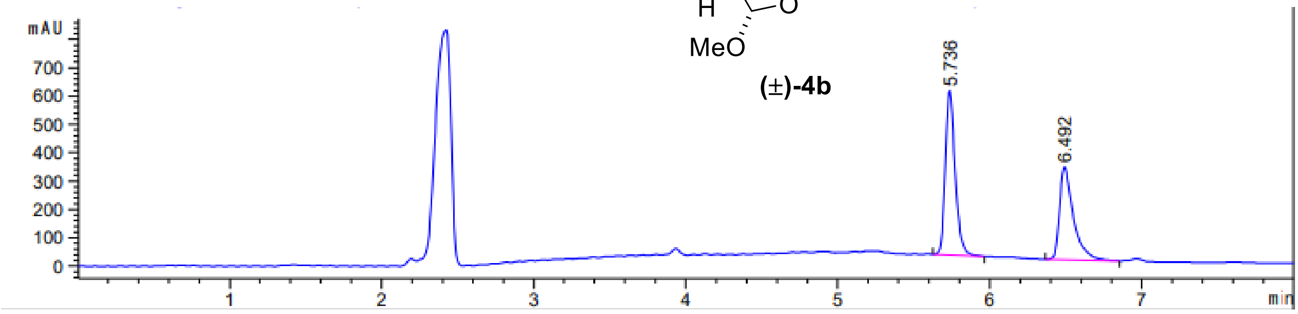
7

Figure S84. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **7**.

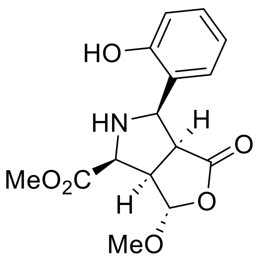
SFC-HPLC traces of cycloadducts 4



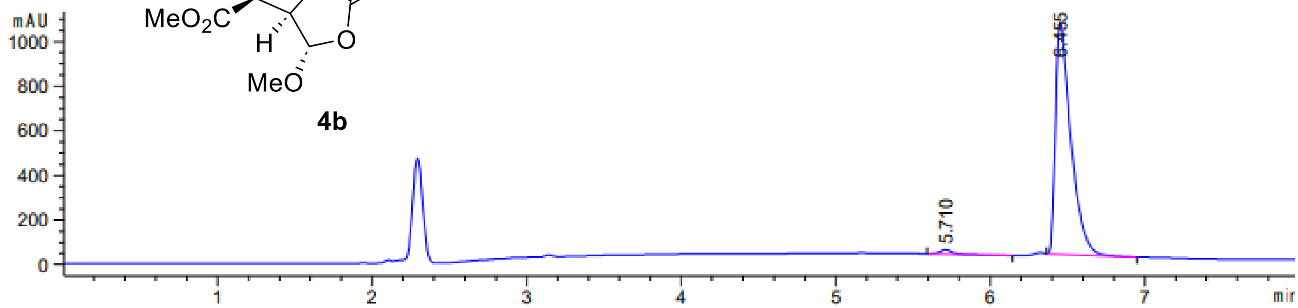
(±)-4b



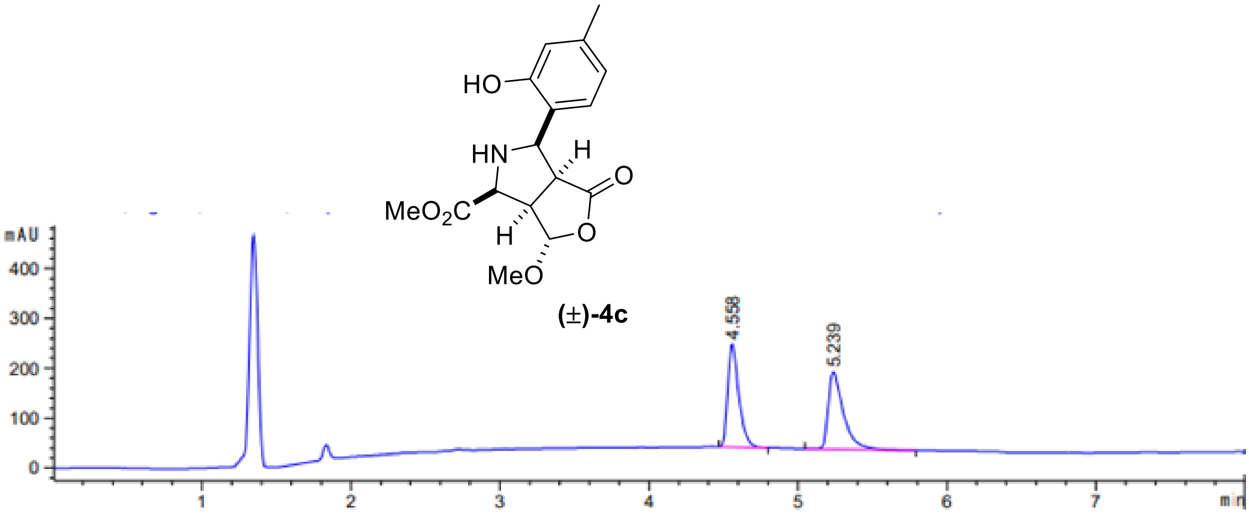
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.736	BB	0.0686	2616.39648	580.33423	55.8965
2	6.492	BB	0.0918	2064.39478	326.27997	44.1035



4b

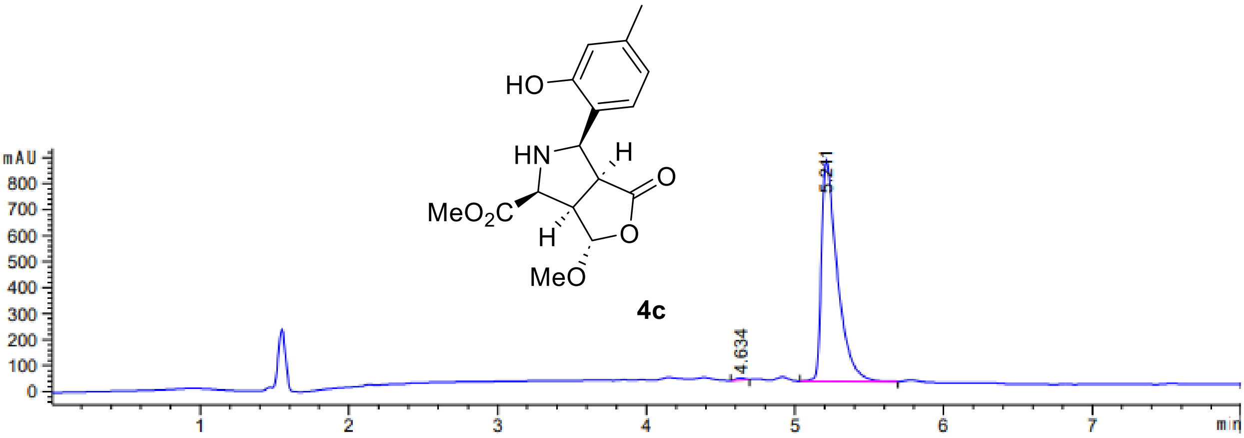


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.710	BB	0.0867	120.90630	20.54099	1.6579
2	6.455	BB	0.1026	7171.72168	1038.71777	98.3421



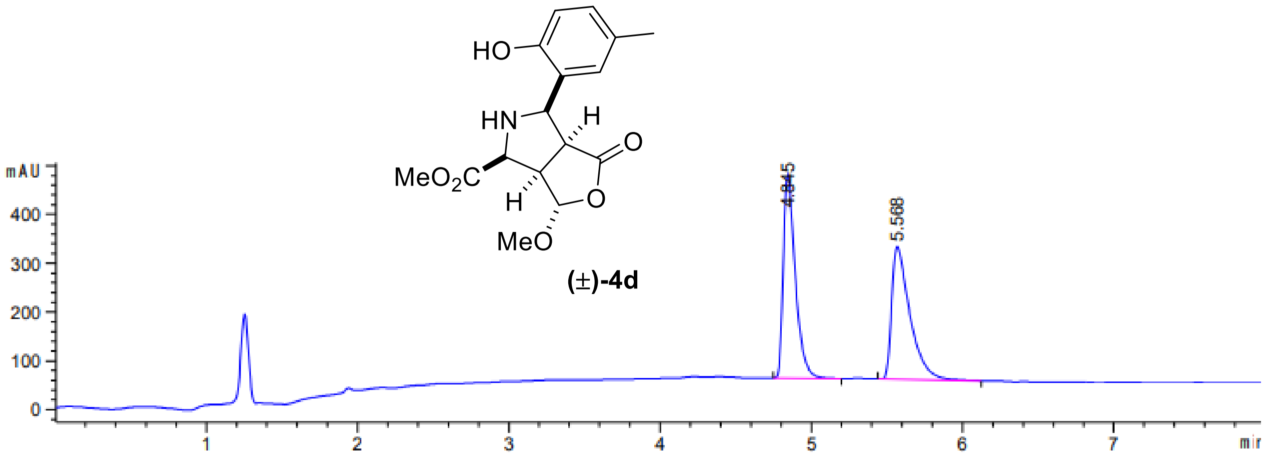
(±)-4c

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.558	BB	0.0779	1058.68726	206.35347	49.0448
2	5.239	BB	0.1052	1099.92419	154.32478	50.9552

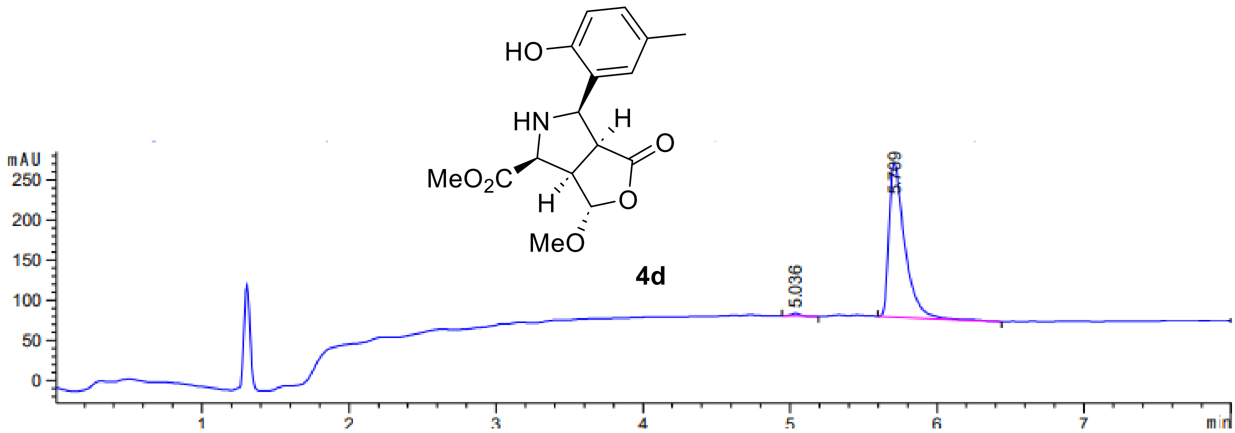


4c

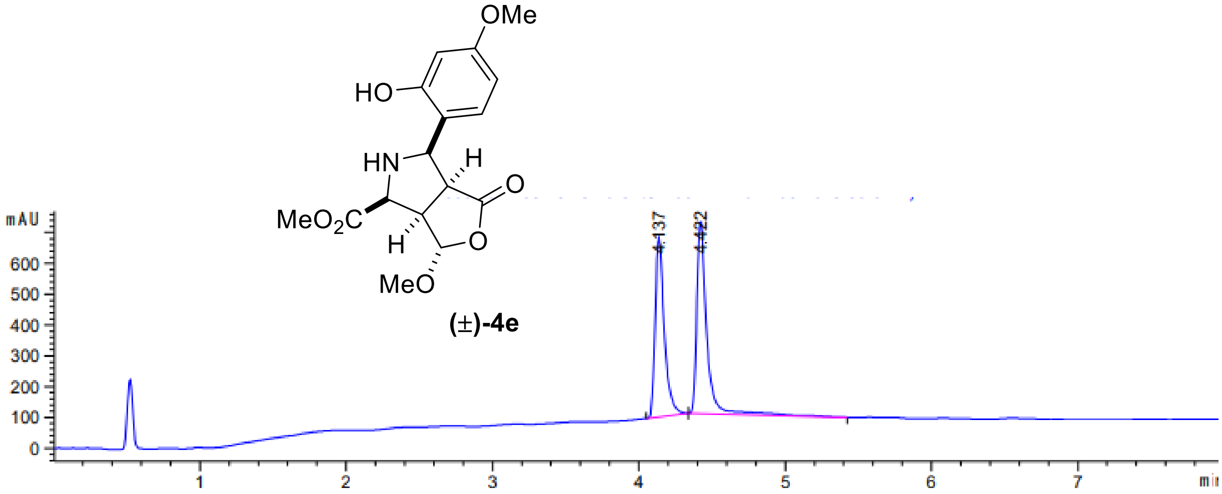
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.634	BB	0.0569	27.30670	7.79204	0.4318
2	5.211	BB	0.1082	6296.65430	852.02948	99.5682



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.845	BB	0.0822	2295.54297	417.29117	50.2135
2	5.568	BB	0.1235	2276.02222	272.27835	49.7865

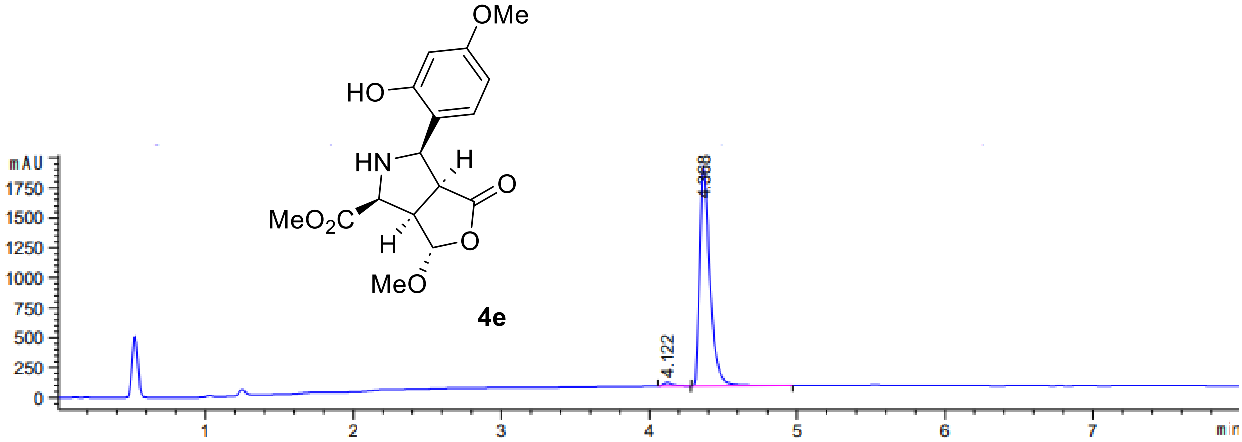


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.036	BB	0.0652	14.72874	3.49230	1.0185
2	5.709	BB	0.1108	1431.42139	192.49759	98.9815



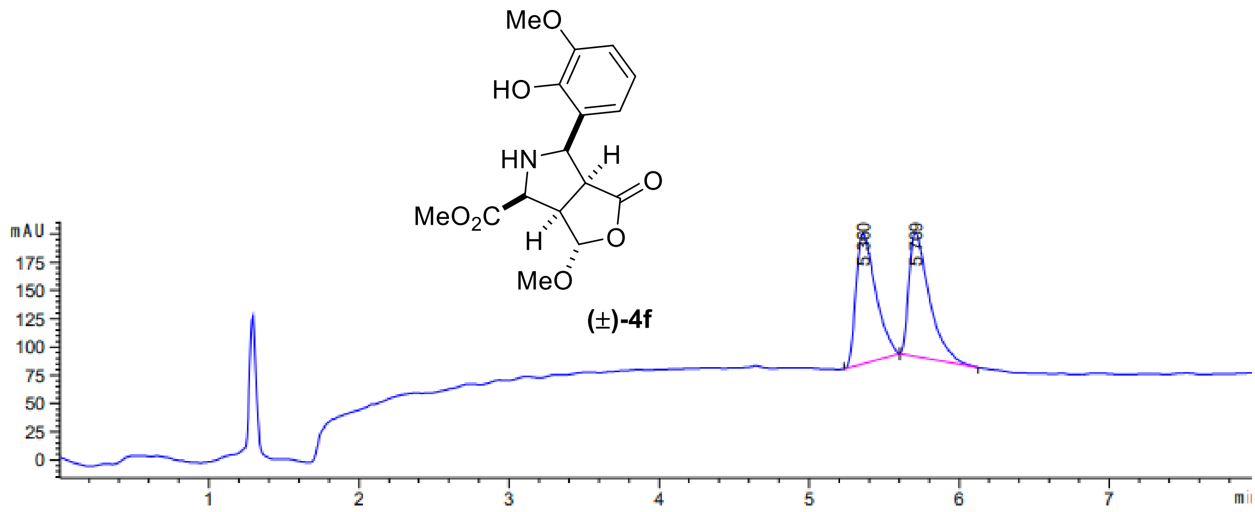
(±)-4e

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.137	BB	0.0648	2535.58667	582.48053	45.8397
2	4.422	BB	0.0699	2995.83960	624.90186	54.1603

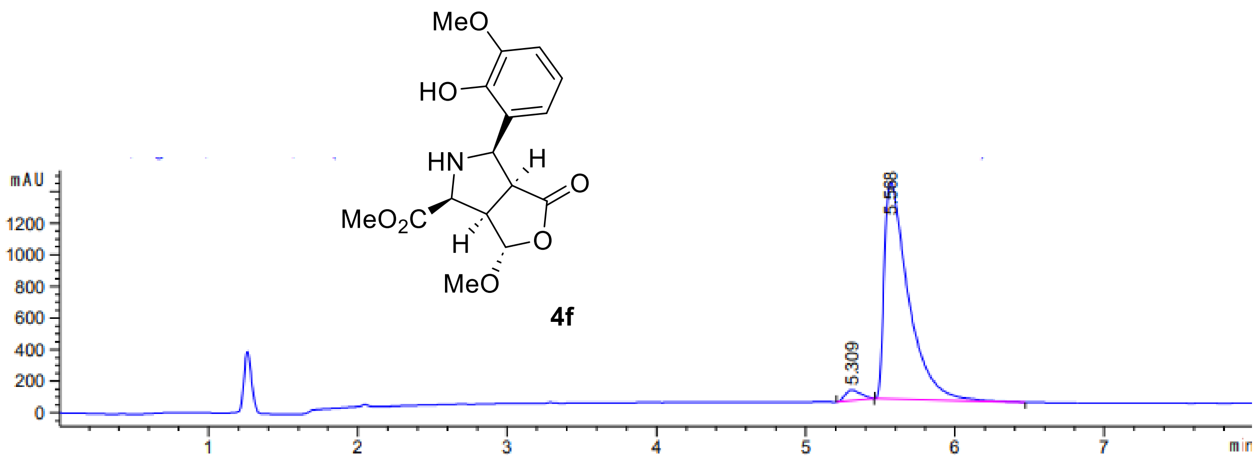


4e

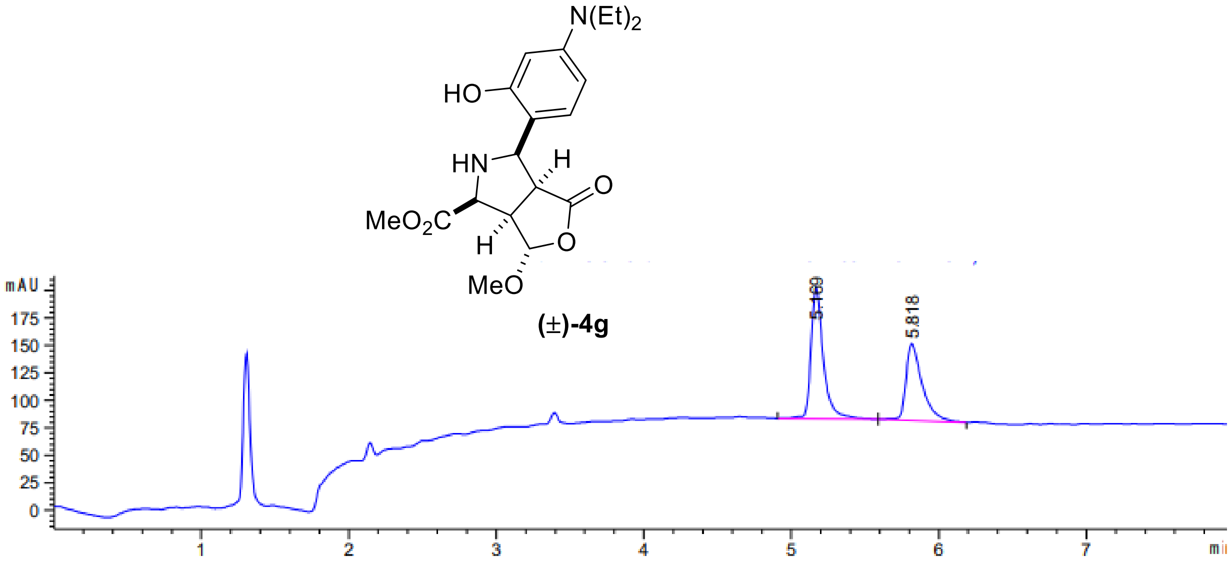
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.122	BB	0.0634	122.03867	28.82069	1.3849
2	4.368	BB	0.0713	8690.03320	1832.78967	98.6151



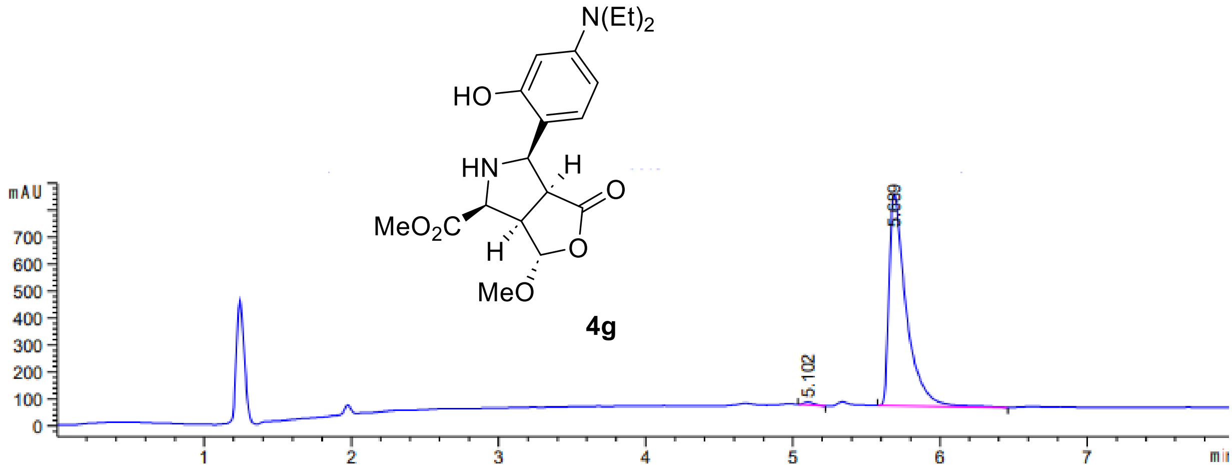
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.360	BB	0.1388	1052.12231	114.93867	50.2576
2	5.709	BB	0.1410	1041.33813	109.40602	49.7424



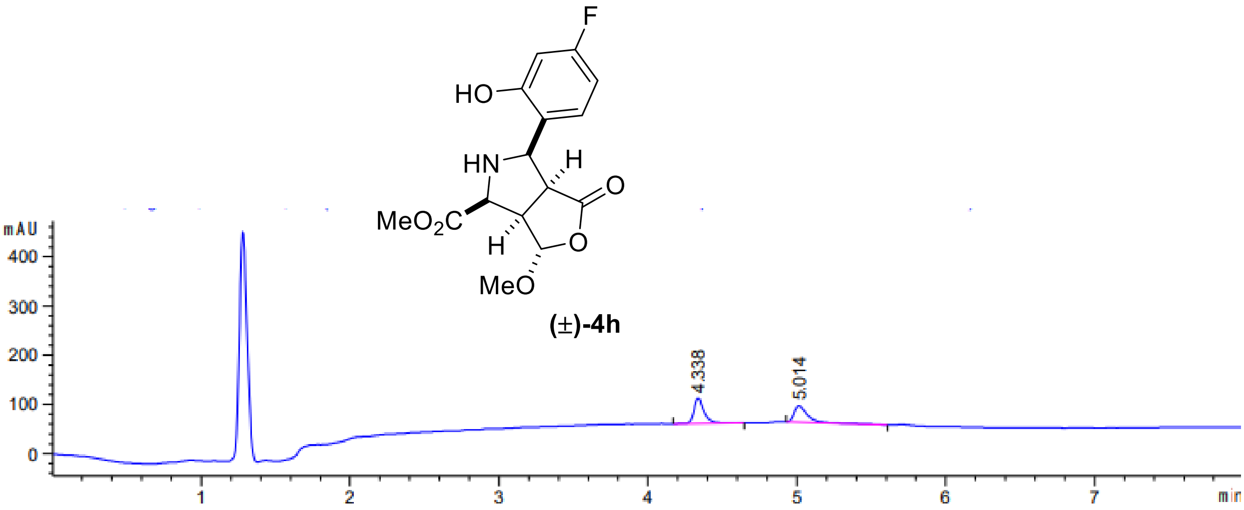
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.309	BB	0.1160	481.98306	65.38141	3.0465
2	5.568	BB	0.1642	1.53388e4	1374.18030	96.9535



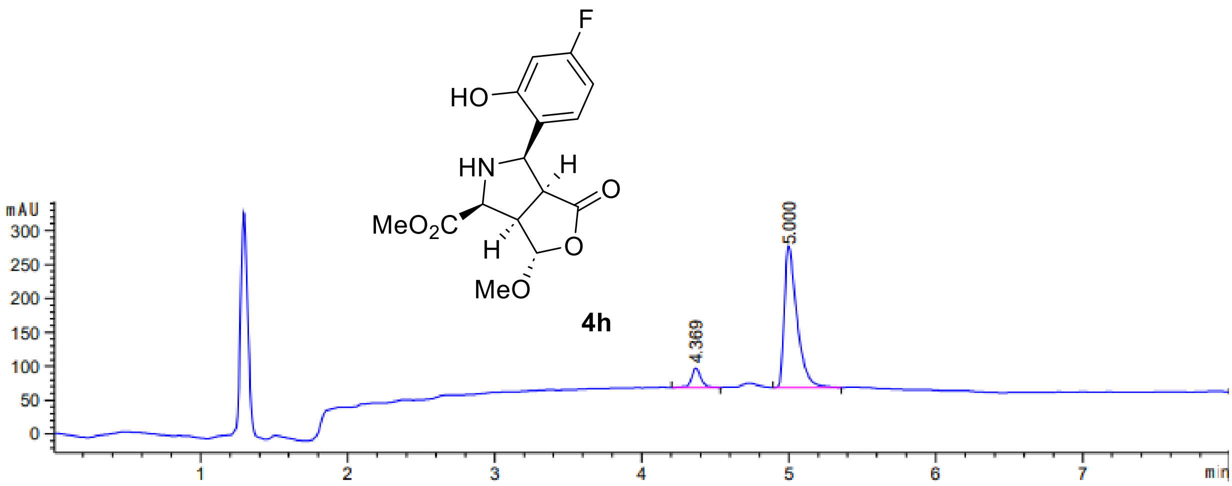
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.169	BB	0.0861	700.65259	119.97691	56.7724
2	5.818	BB	0.1132	533.49030	69.79887	43.2276



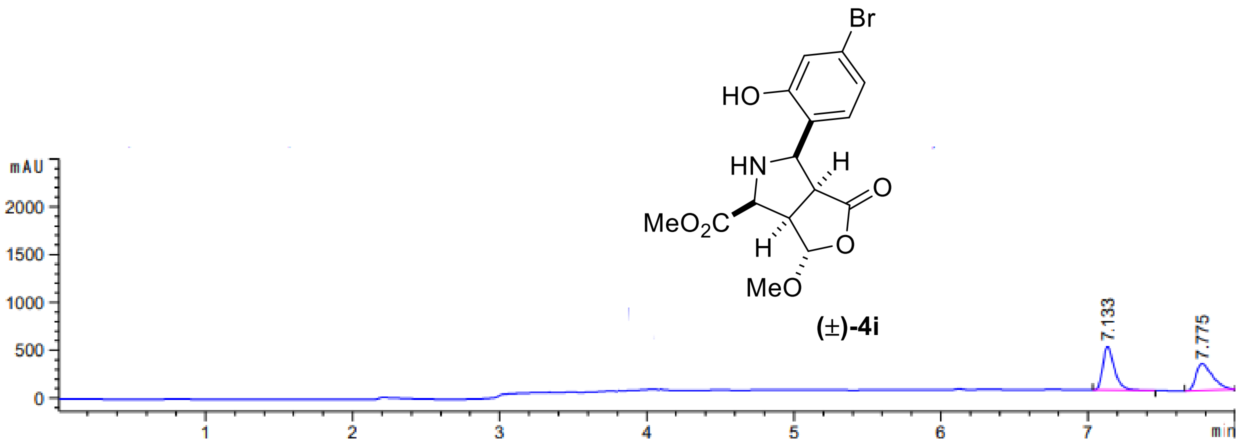
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.102	BB	0.0758	52.32770	10.93172	0.8218
2	5.689	BB	0.1179	6314.90869	784.72107	99.1782



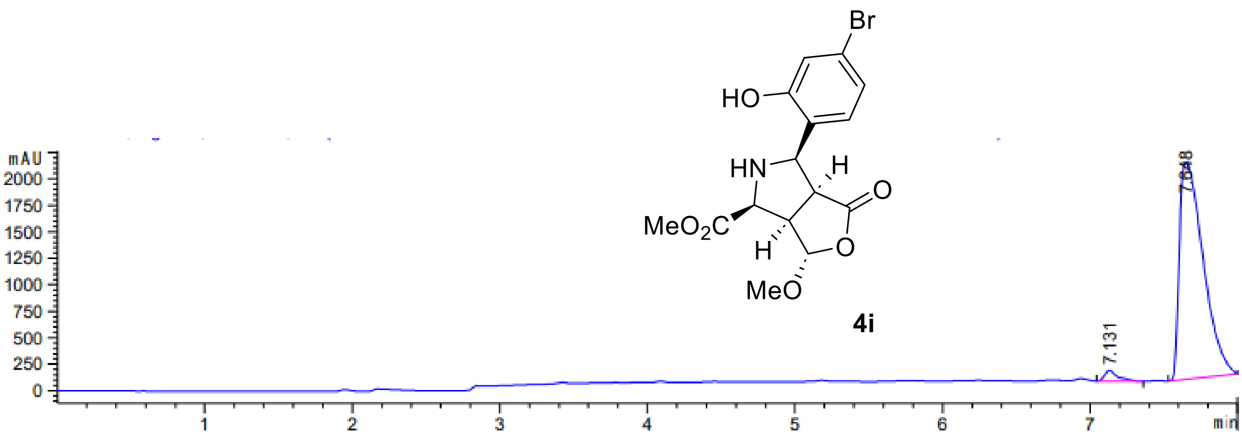
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.338	BB	0.0685	239.95529	51.33878	51.5016
2	5.014	BB	0.0978	225.96268	33.89556	48.4984



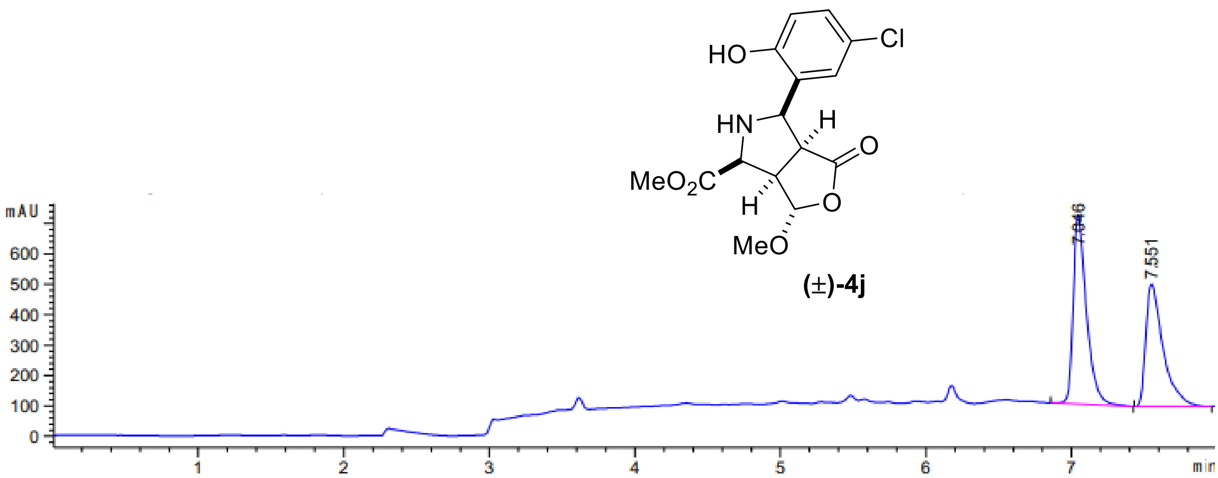
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.369	BB	0.0664	121.22521	28.06443	8.9298
2	5.000	BB	0.0891	1236.31091	208.82001	91.0702



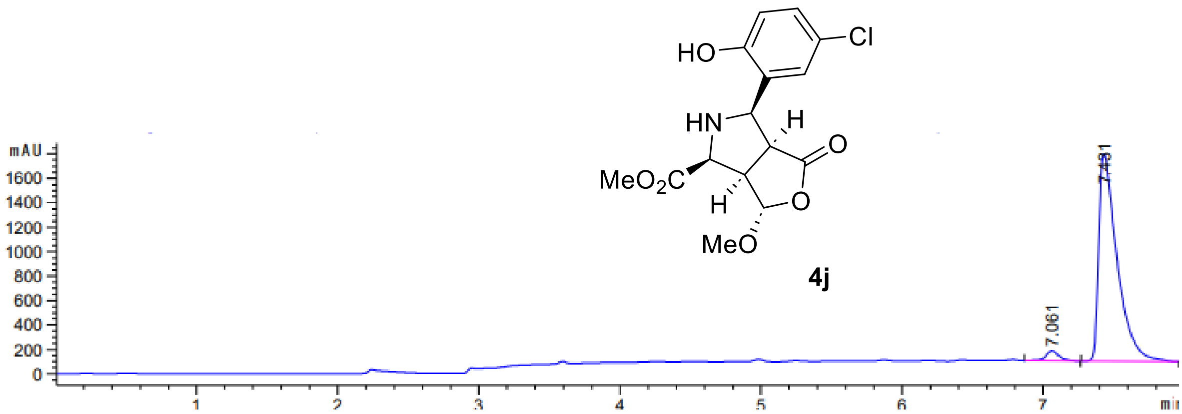
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.133	BB	0.0841	2513.83691	457.30008	53.2397
2	7.775	BBA	0.1178	2207.89526	280.58603	46.7603



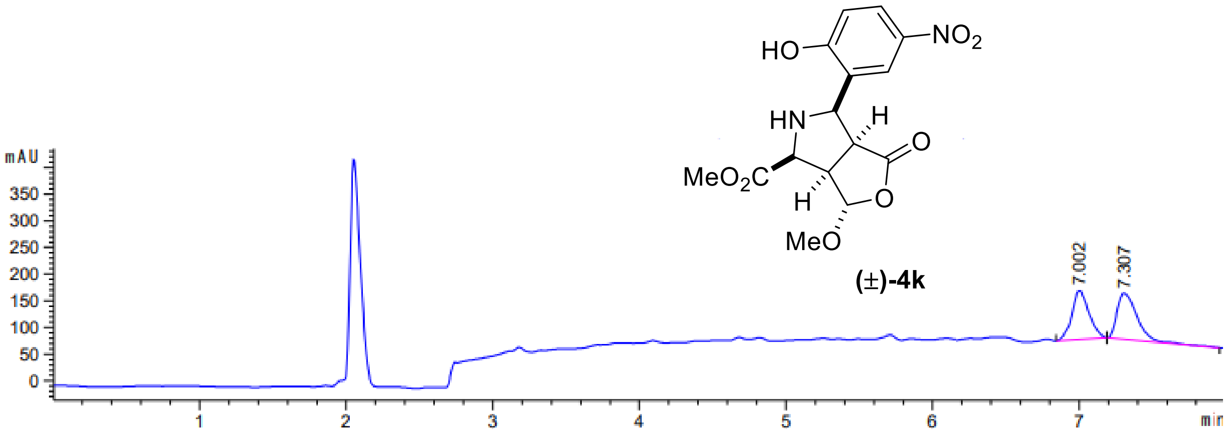
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.131	BB	0.0915	626.37134	99.40401	2.6731
2	7.648	BBA	0.1738	2.28056e4	2050.48608	97.3269



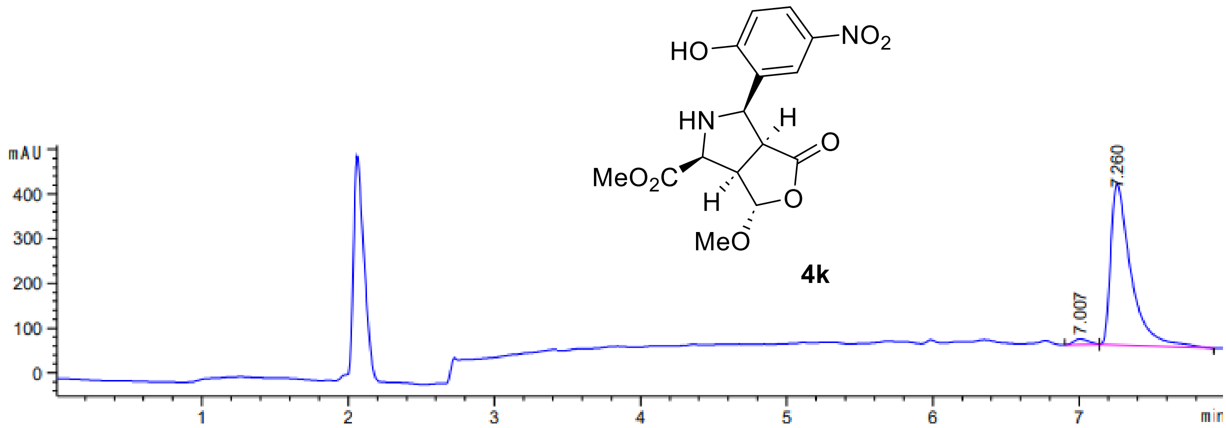
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.046	BB	0.0940	3957.43066	624.23914	54.2382
2	7.551	BBA	0.1227	3338.96387	402.93973	45.7618



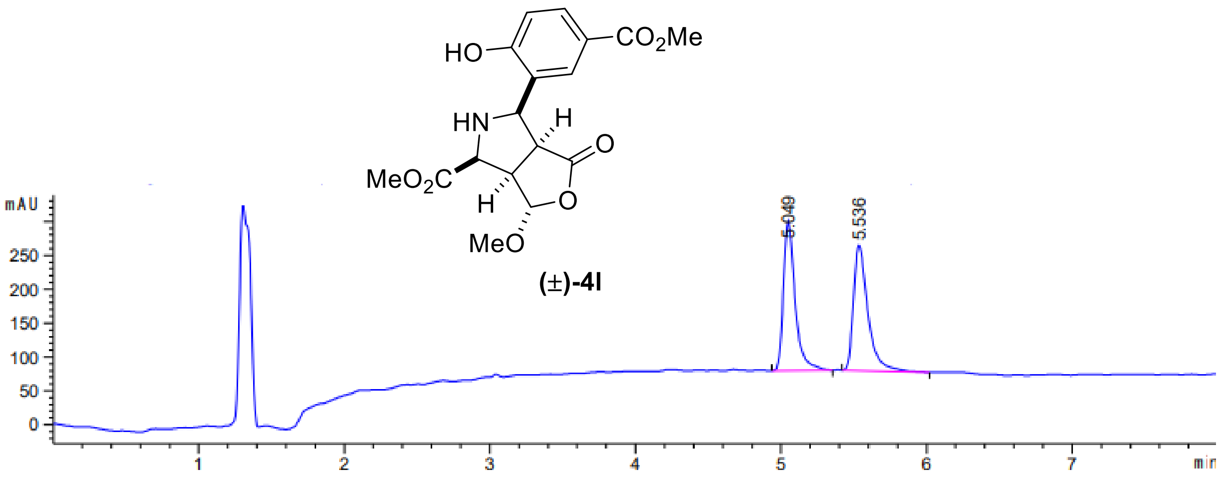
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.061	BB	0.0979	543.06860	81.29294	3.4424
2	7.431	BB	0.1326	1.52329e4	1698.23926	96.5576



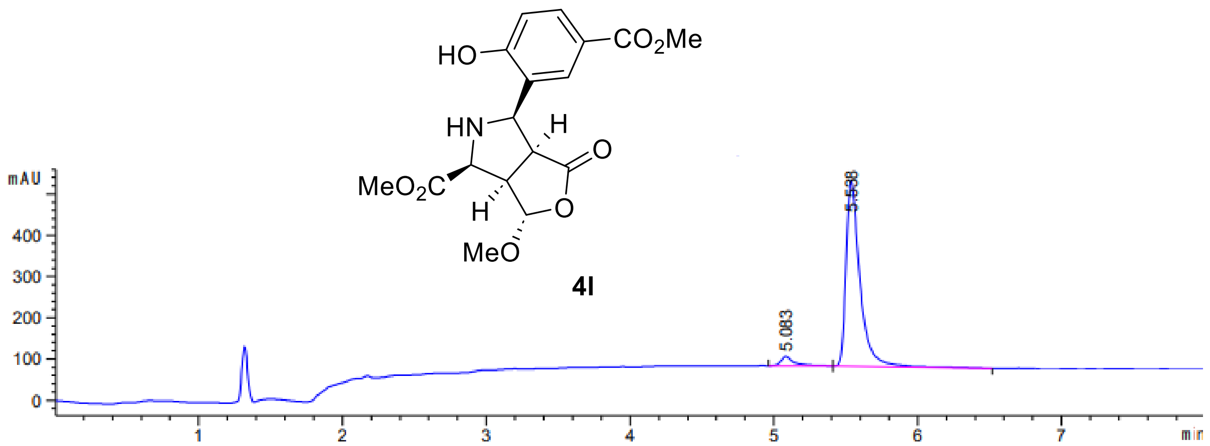
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.002	BB	0.1201	739.17505	91.65948	47.4253
2	7.307	BB	0.1510	819.43323	86.12552	52.5747



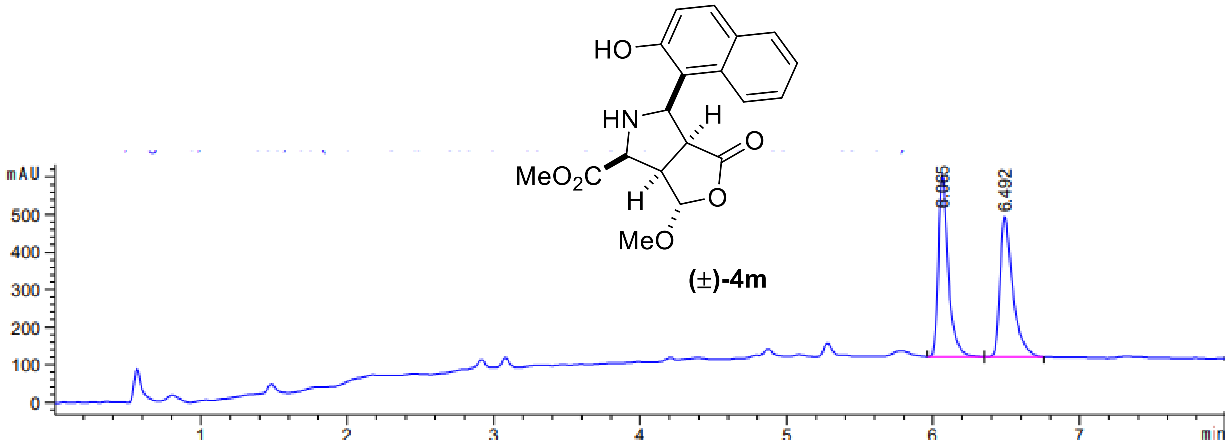
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.007	BB	0.1118	89.30550	12.74031	2.5021
2	7.260	BBA	0.1404	3479.97266	361.05930	97.4979



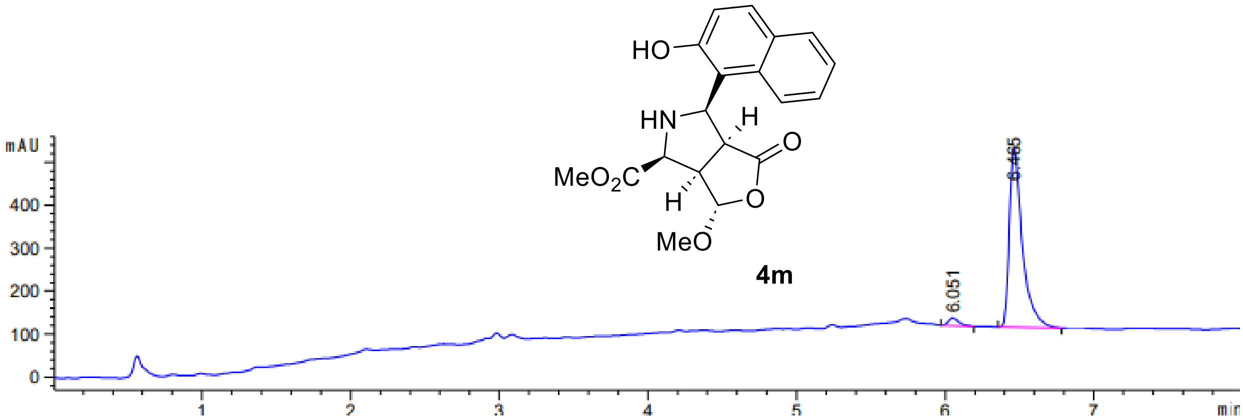
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.049	BB	0.0830	1227.92810	220.44093	49.0470
2	5.536	BB	0.1026	1275.64819	184.53412	50.9530



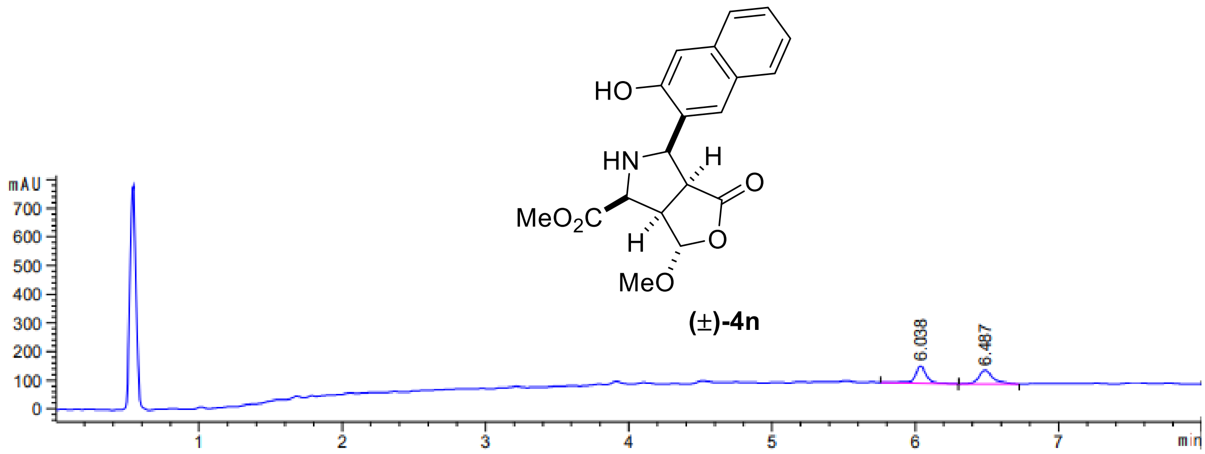
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.083	BB	0.0910	137.75325	22.02518	4.3500
2	5.538	BB	0.0984	3028.96338	450.68890	95.6500



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.065	BB	0.0691	2282.36011	482.87964	50.5393
2	6.492	BB	0.0877	2233.64868	374.08179	49.4607

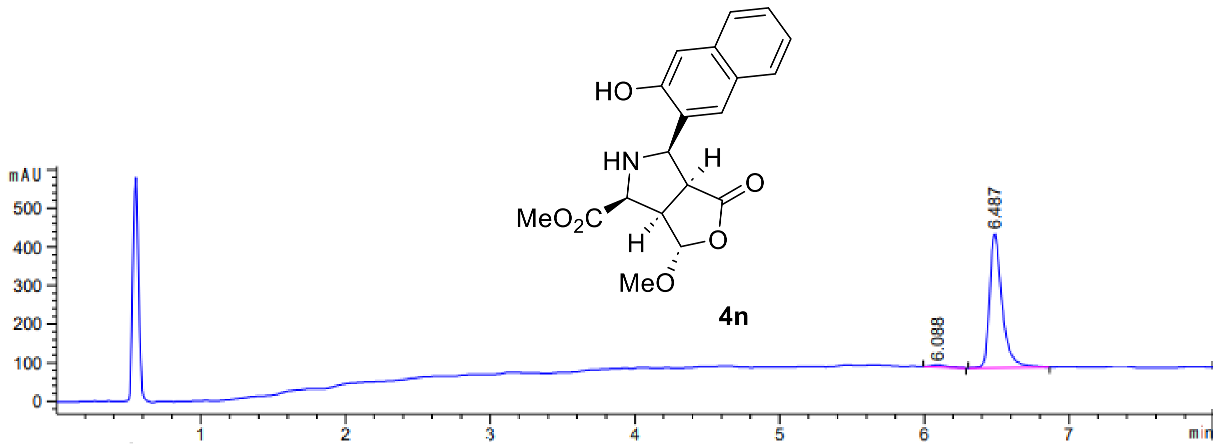


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.051	BB	0.0730	87.97845	17.99936	3.3819
2	6.465	BB	0.0881	2513.49194	418.18091	96.6181



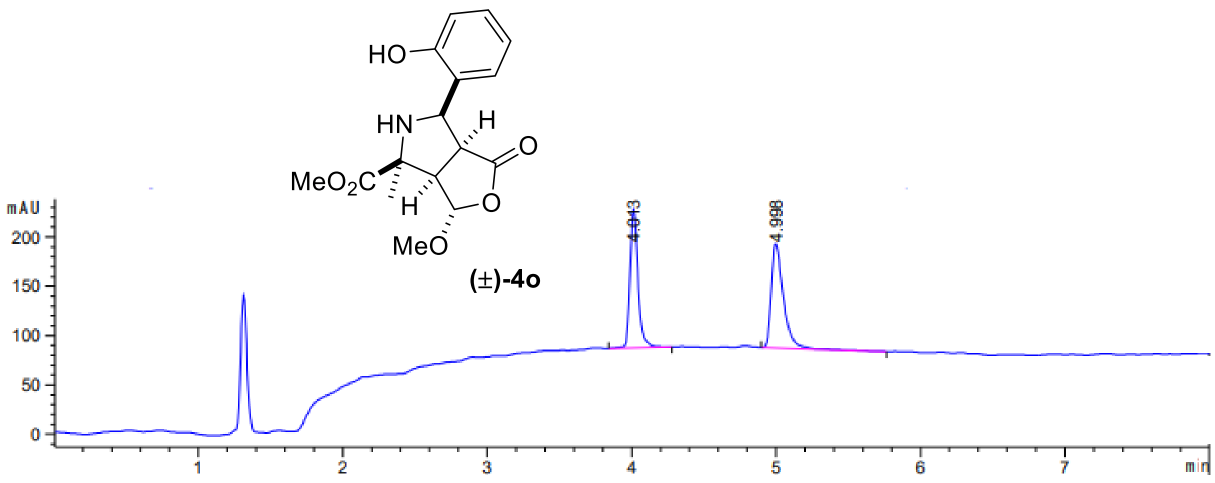
(±)-4n

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.038	BB	0.0818	341.79257	60.61693	50.6615
2	6.487	BB	0.1010	332.86655	47.94144	49.3385

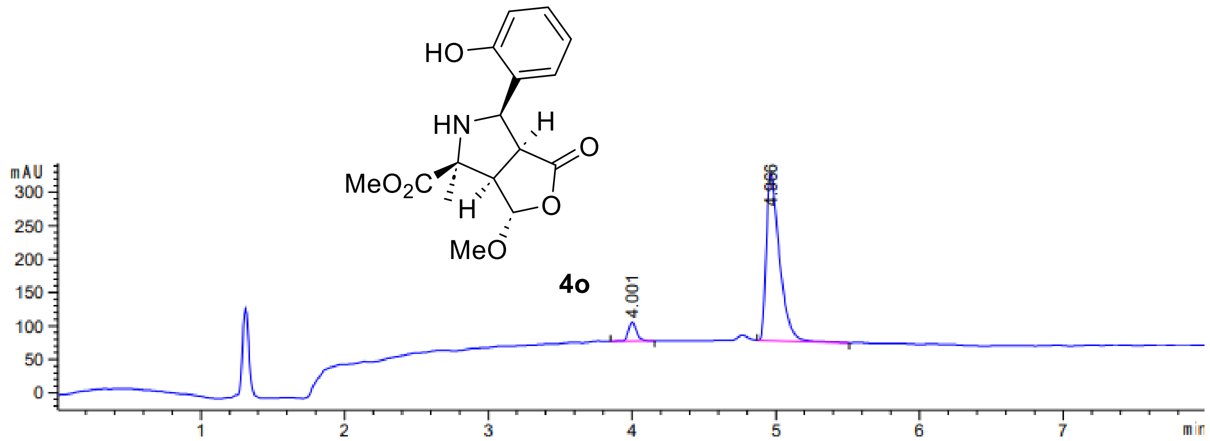


4n

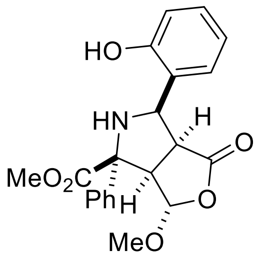
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.088	BB	0.0951	36.09954	5.46423	1.7161
2	6.487	BB	0.0896	2067.51270	346.35199	98.2839



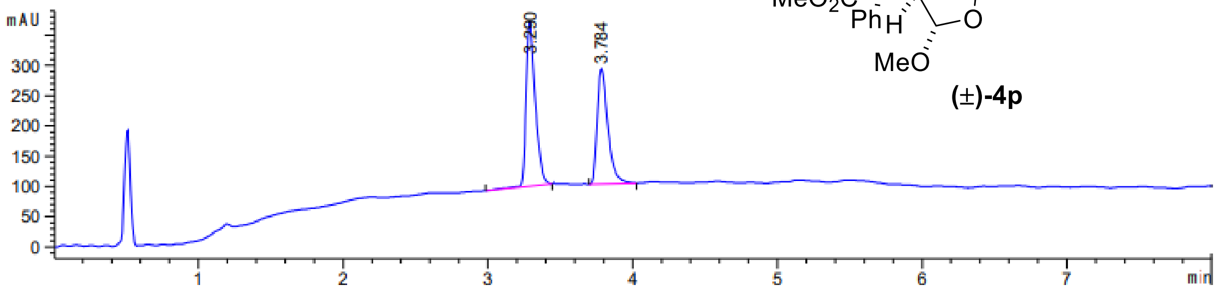
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.013	BB	0.0589	538.08643	139.68153	46.6384
2	4.998	BB	0.0880	615.65424	105.68761	53.3616



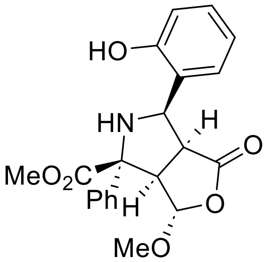
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.001	BB	0.0597	112.80188	28.81614	6.6294
2	4.966	BB	0.0944	1588.74573	249.13206	93.3706



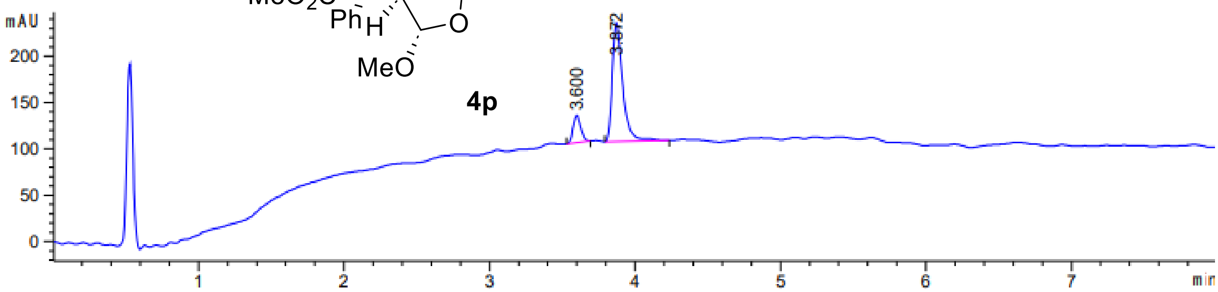
(±)-4p



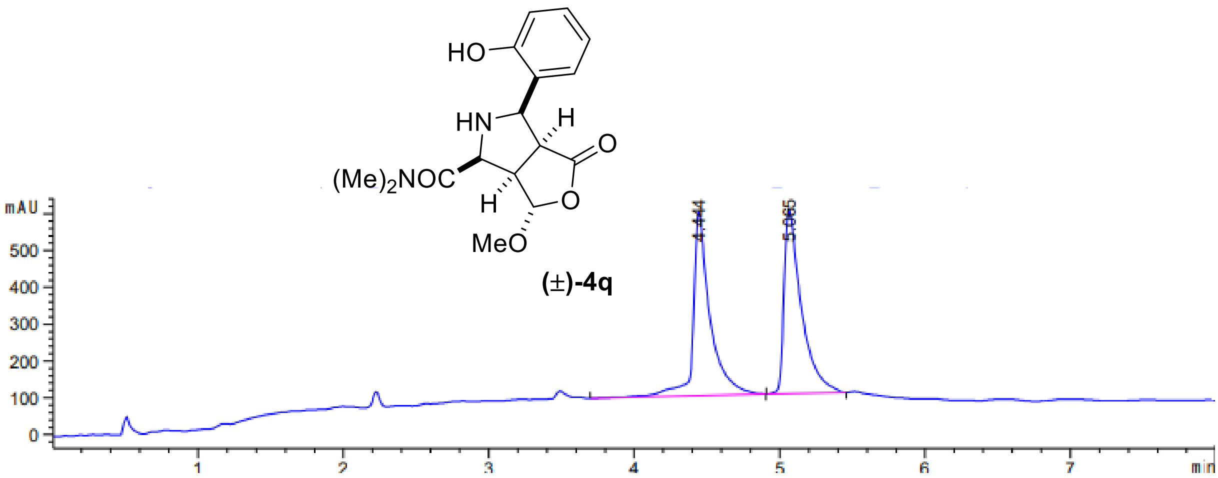
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.290	BB	0.0649	1192.72998	273.64426	54.9658
2	3.784	BB	0.0779	977.22021	190.29283	45.0342



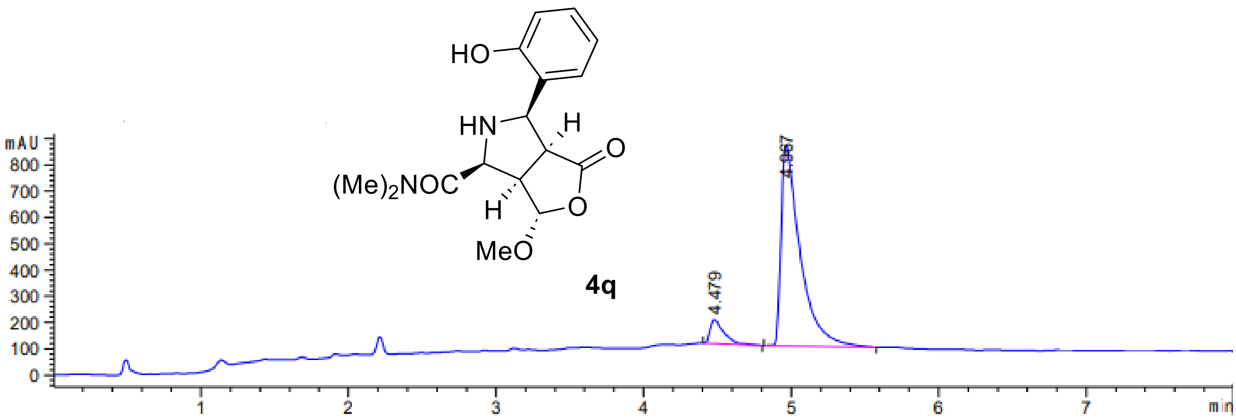
4p



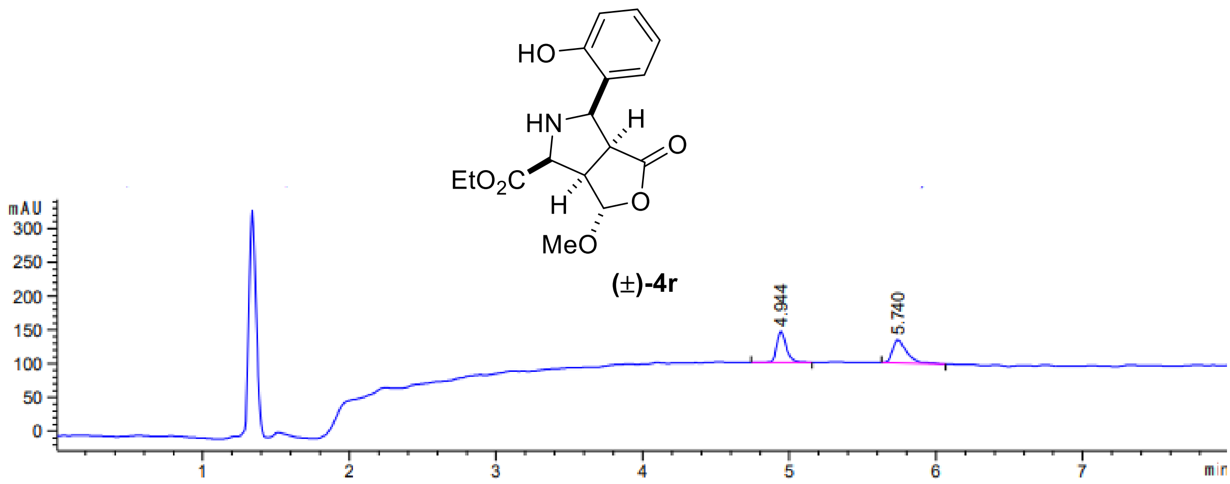
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.600	BB	0.0566	107.60847	29.49168	14.4796
2	3.872	BB	0.0760	635.56671	127.74203	85.5204



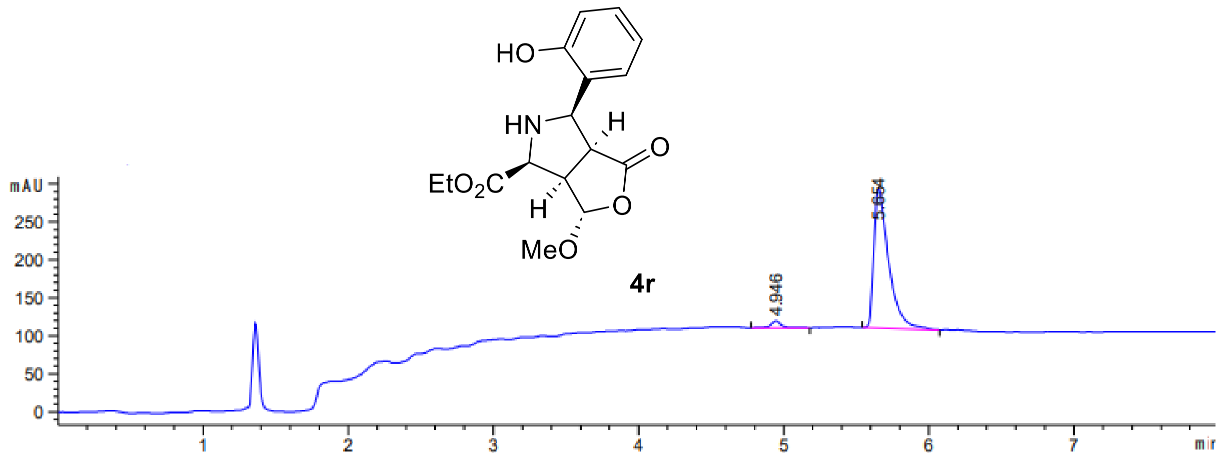
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.444	BB	0.1127	4048.04419	498.48538	49.4924
2	5.065	BB	0.1184	4131.08447	500.07193	50.5076



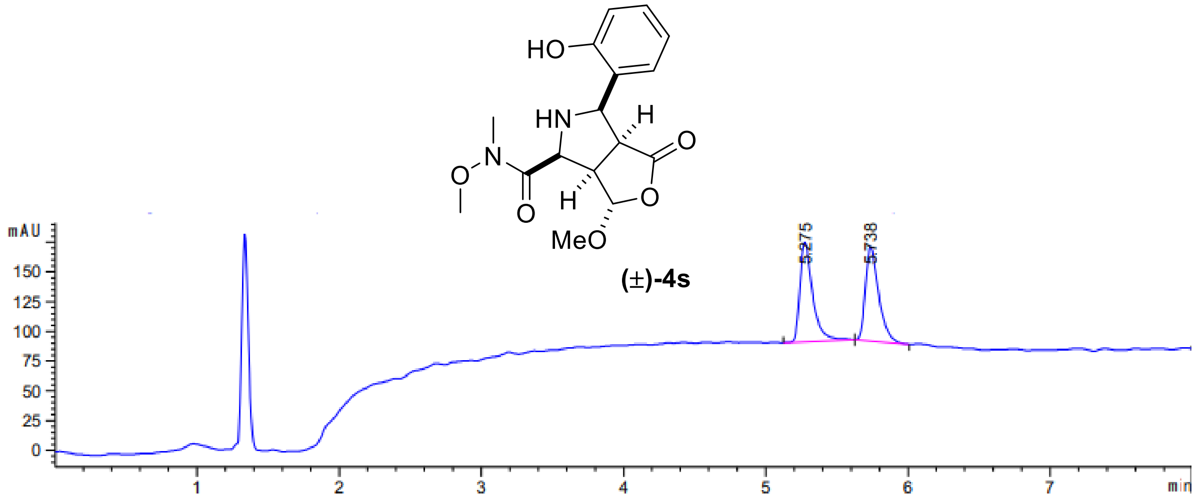
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.479	BB	0.0934	591.62152	91.55354	7.9405
2	4.967	BB	0.1286	6859.05225	765.21808	92.0595



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.944	BB	0.0697	211.99269	46.04057	47.4768
2	5.740	BB	0.1048	234.52547	33.85569	52.5232

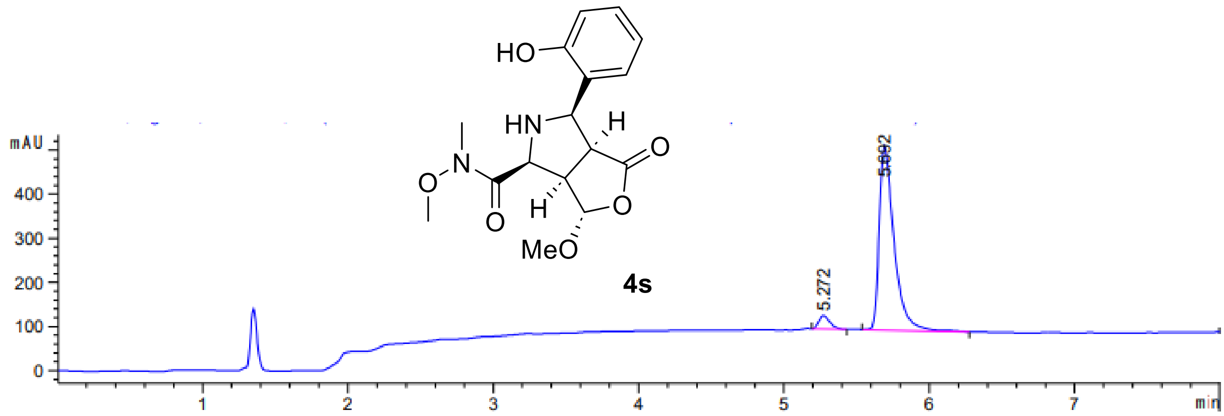


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.946	BB	0.0715	45.18477	9.16427	3.3754
2	5.654	BB	0.1039	1293.47839	184.34502	96.6246



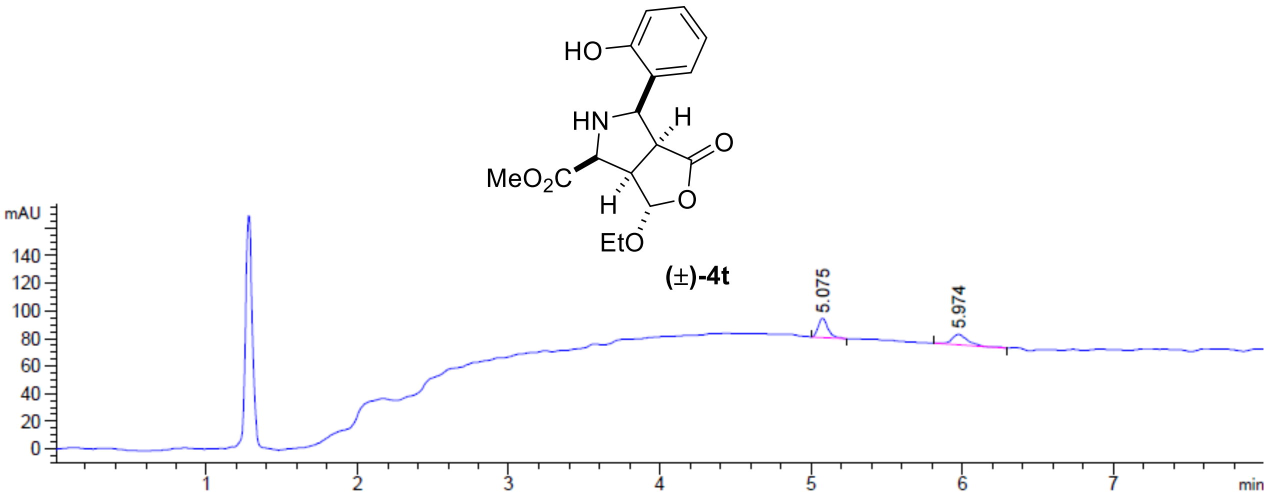
(±)-4s

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.275	BB	0.0930	520.97668	83.26897	50.0646
2	5.738	BB	0.0985	519.63190	79.24296	49.9354



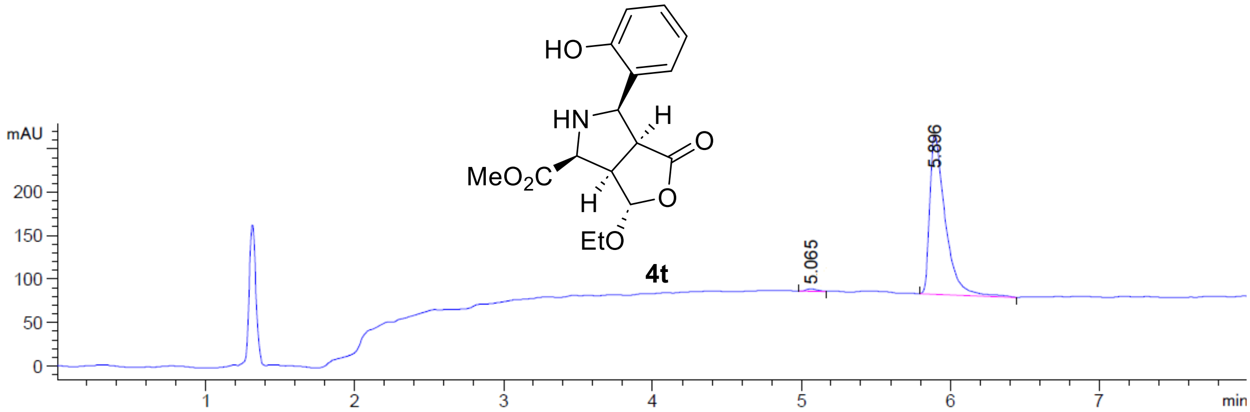
4s

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.272	BB	0.0841	160.96059	30.21964	5.1420
2	5.692	BB	0.1049	2969.34058	417.75375	94.8580

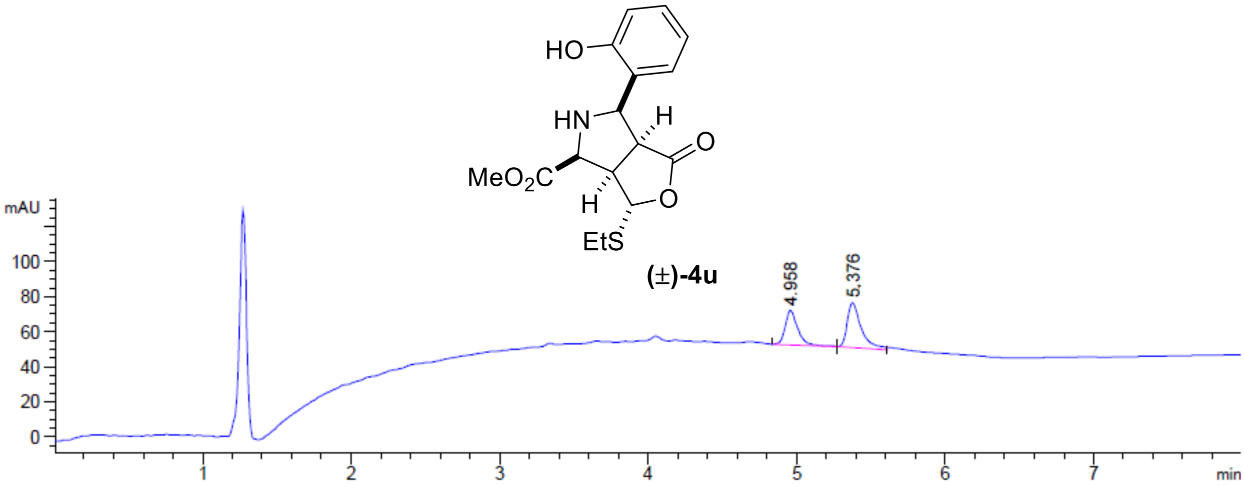


(±)-4t

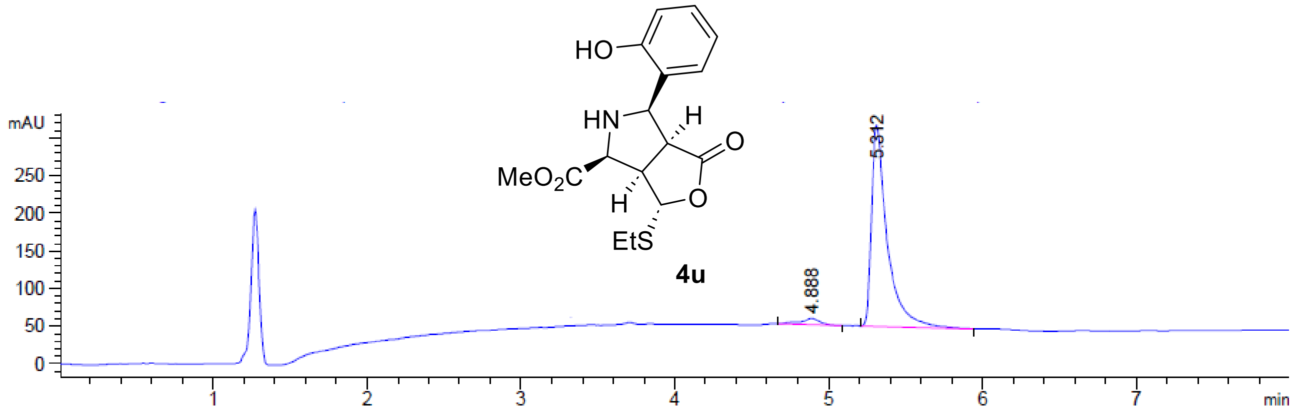
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.075	BB	0.0677	62.63266	14.13878	52.1870
2	5.974	BB	0.1124	57.38316	7.57474	47.8130



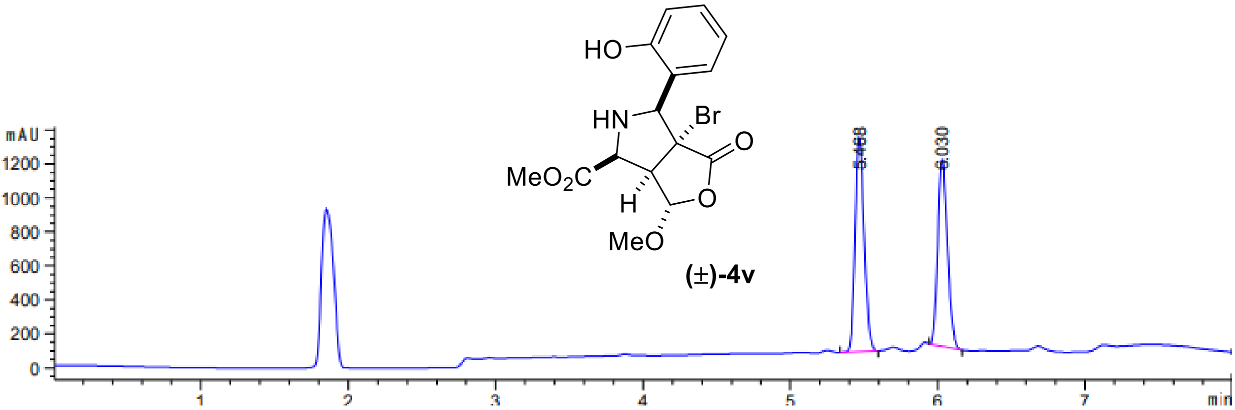
4t



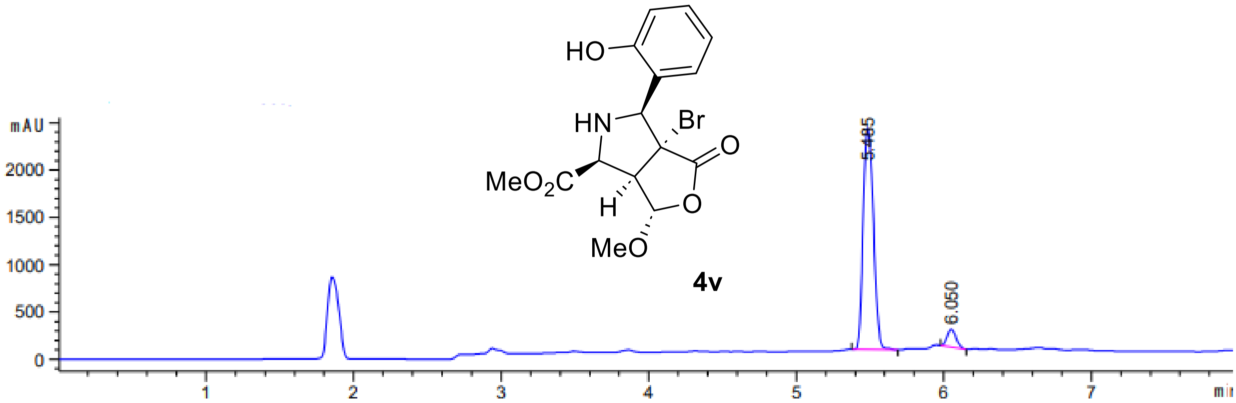
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.958	BB	0.0856	113.61006	19.59394	40.2134
2	5.376	BB	0.1092	168.90775	25.78253	59.7866



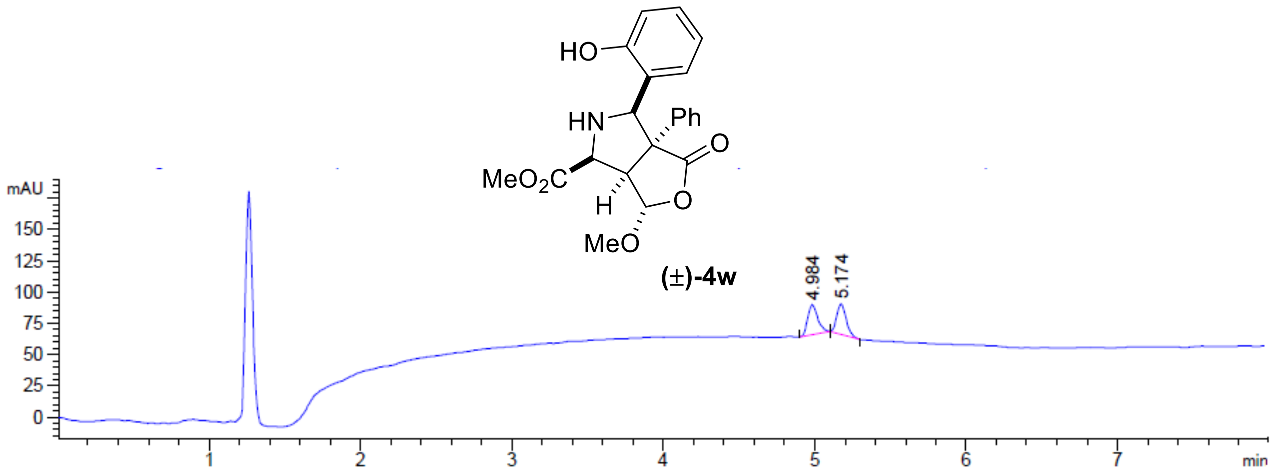
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.888	BB	0.1200	77.11693	8.99960	3.9214
2	5.312	BB	0.1027	1889.43579	266.66891	96.0786



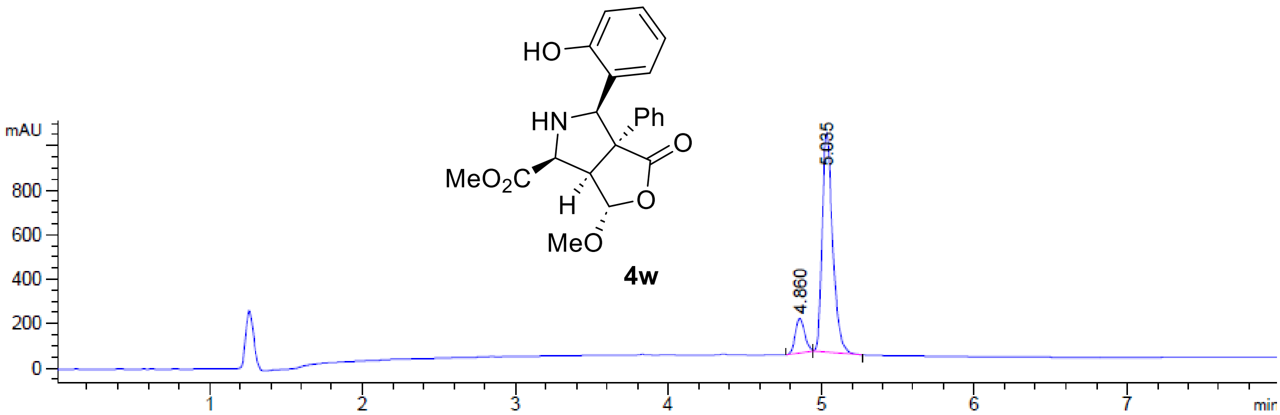
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.468	BB	0.0661	5404.93311	1258.92371	51.8650
2	6.030	BB	0.0691	5016.23047	1102.26428	48.1350



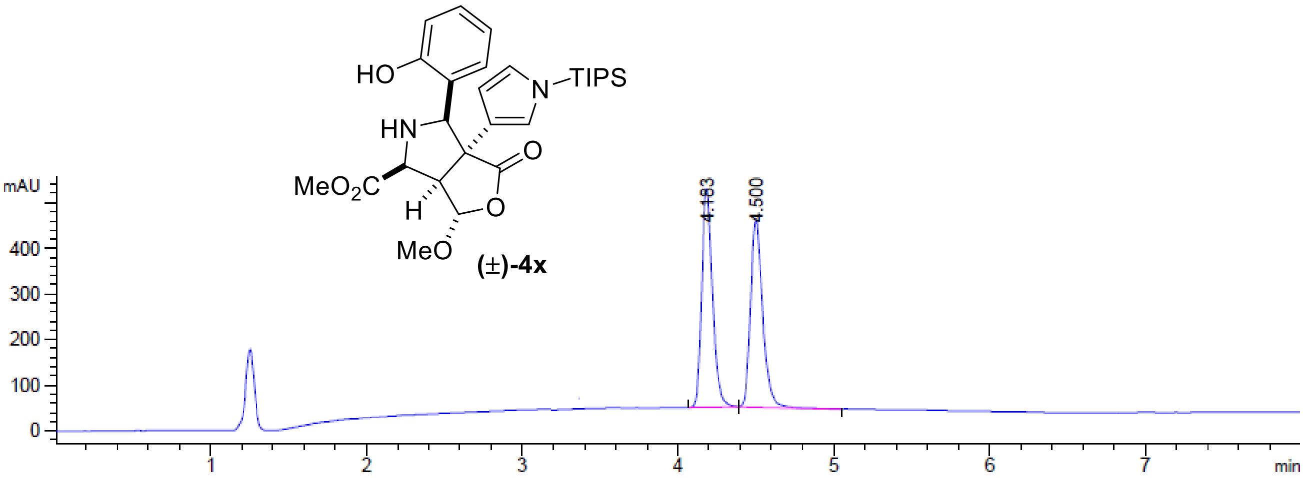
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.485	BB	0.0782	1.12599e4	2335.94141	93.4759
2	6.050	BB	0.0668	785.87988	187.83875	6.5241



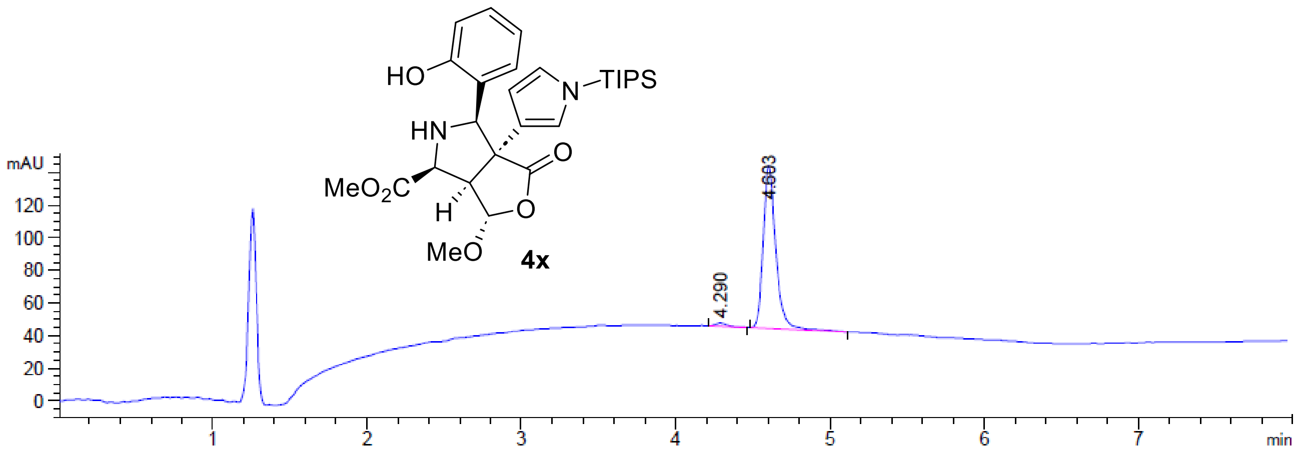
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.984	BB	0.0694	109.85074	24.01087	51.2326
2	5.174	BB	0.0661	104.56509	24.33723	48.7674



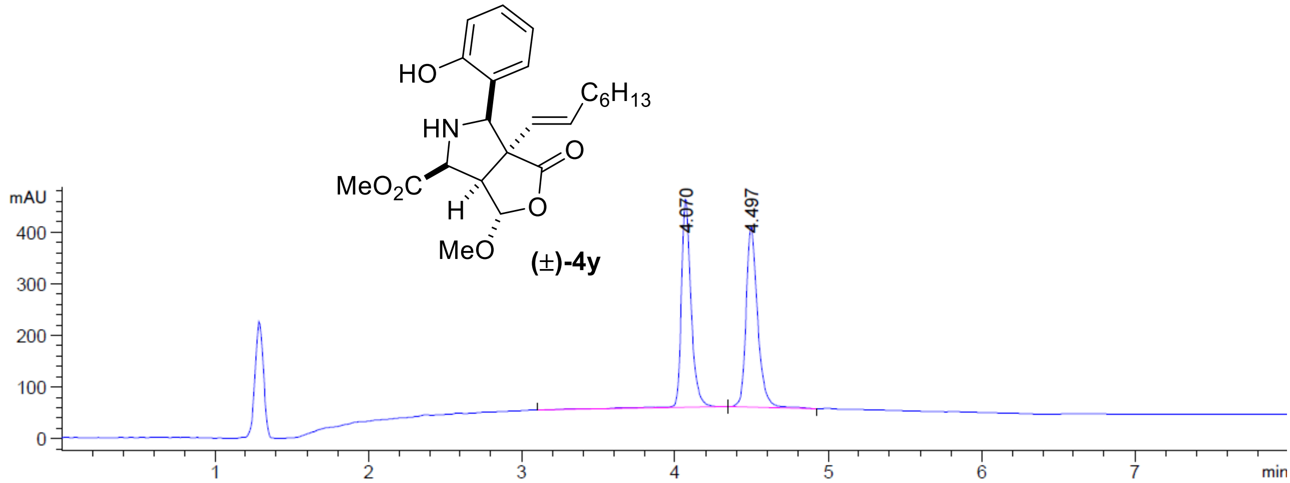
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.860	BB	0.0658	665.49341	155.94643	12.3854
2	5.035	BB	0.0715	4707.72461	989.53674	87.6146



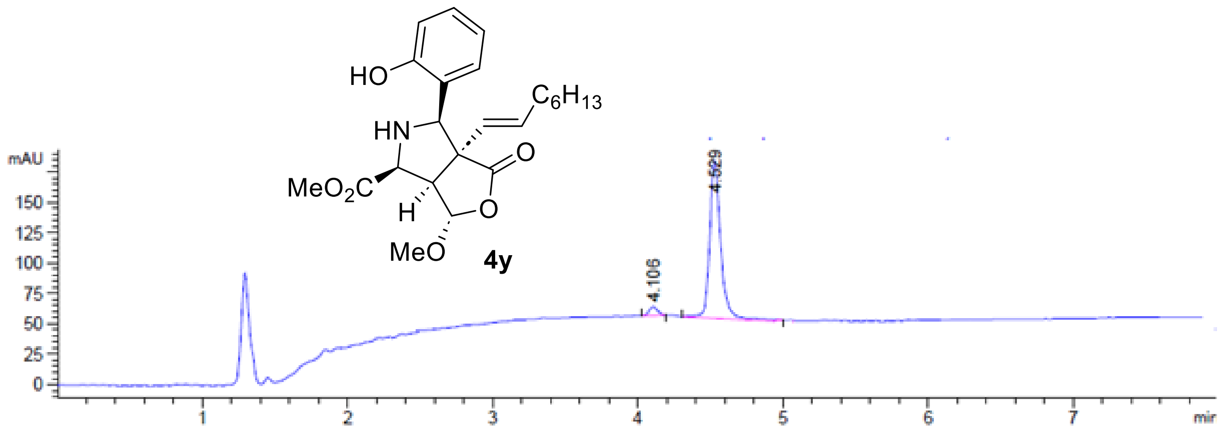
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.183	BB	0.0741	2315.54395	481.87674	50.9871
2	4.500	BB	0.0814	2225.88501	409.65826	49.0129



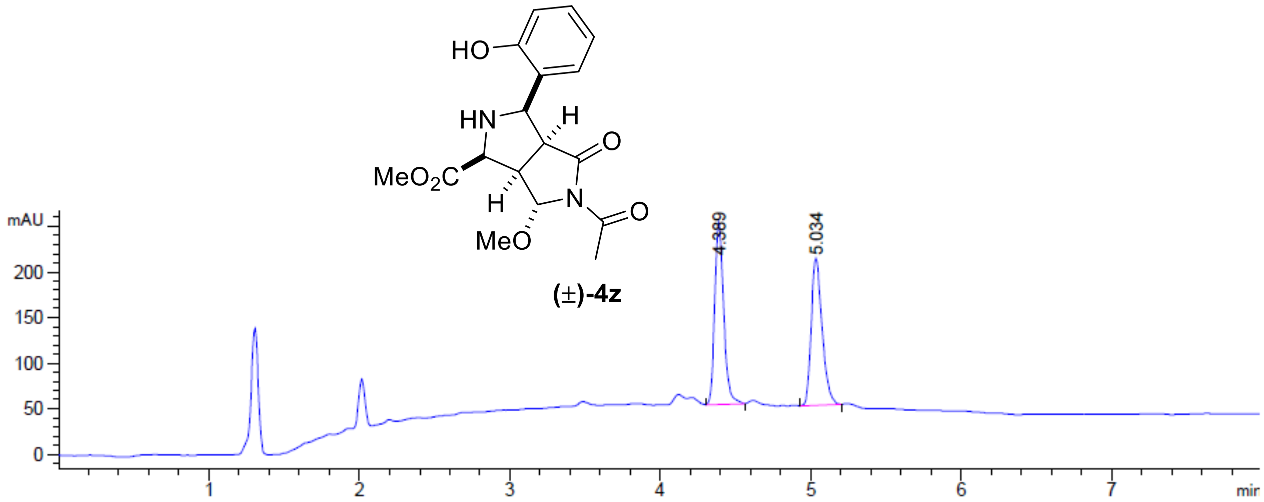
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.290	BB	0.0728	9.98764	1.98111	1.7476
2	4.603	BB	0.0856	561.51184	99.82718	98.2524



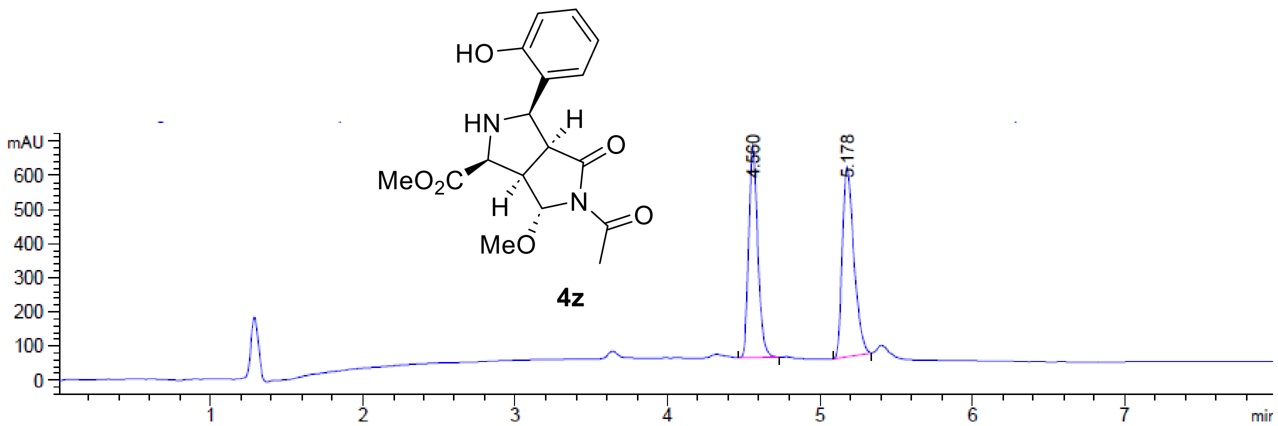
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.070	BB	0.0659	1805.53894	405.62766	49.6948
2	4.497	BB	0.0787	1827.71887	351.26193	50.3052



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.106	BB	0.0614	28.28265	7.27486	3.5926
2	4.529	BB	0.0865	758.96509	129.27345	96.4074



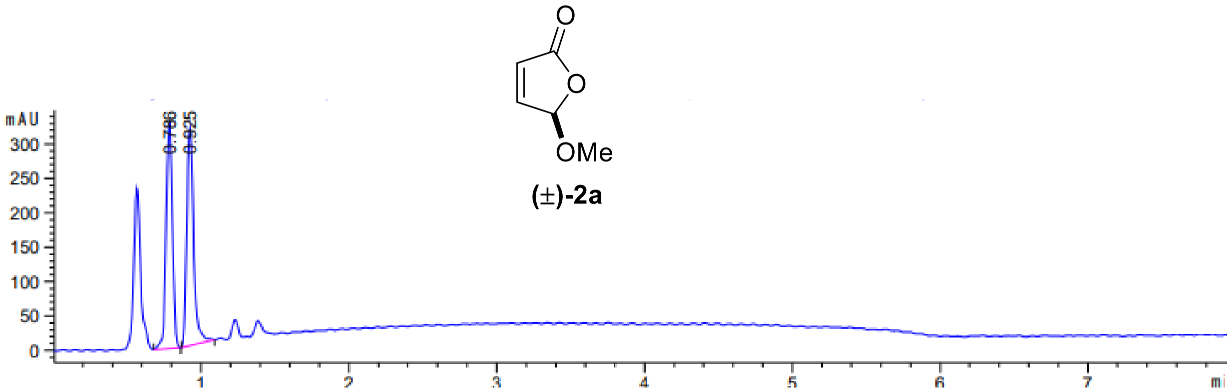
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.389	BB	0.0621	823.09399	199.70868	50.4694
2	5.034	BB	0.0765	807.78320	161.15132	49.5306



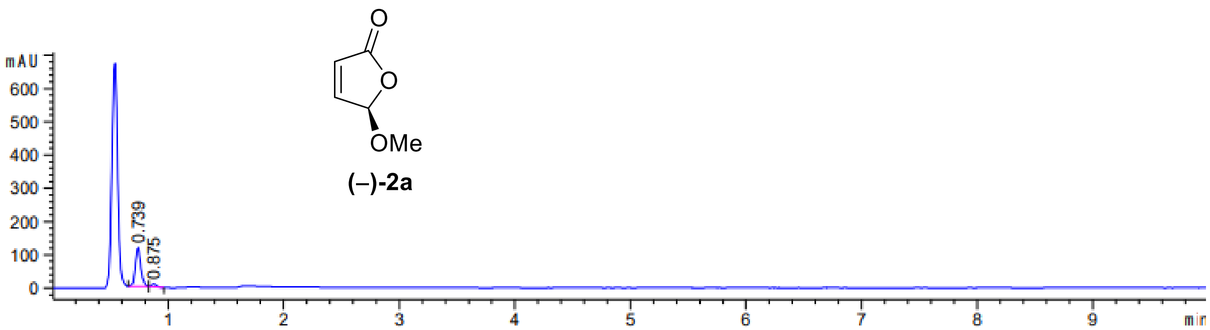
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.560	BB	0.0643	2576.74170	622.49231	46.6716
2	5.178	BB	0.0817	2944.26538	556.41541	53.3284

SFC-HPLC traces of furanones 2

KR of (±)-2a from 4b:

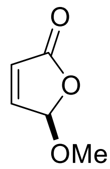


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.786	BB	0.0465	975.98798	330.43430	48.9923
2	0.925	BB	0.0493	1016.13629	317.94958	51.0077

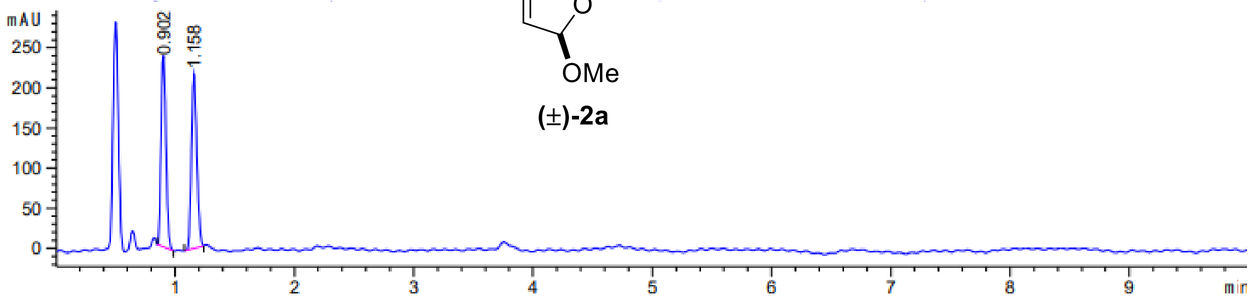


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.739	BB	0.0507	385.51190	116.33720	93.5051
2	0.875	BB	0.0471	26.77774	8.90522	6.4949

KR of (±)-2a from 4b (1 mmol scale):

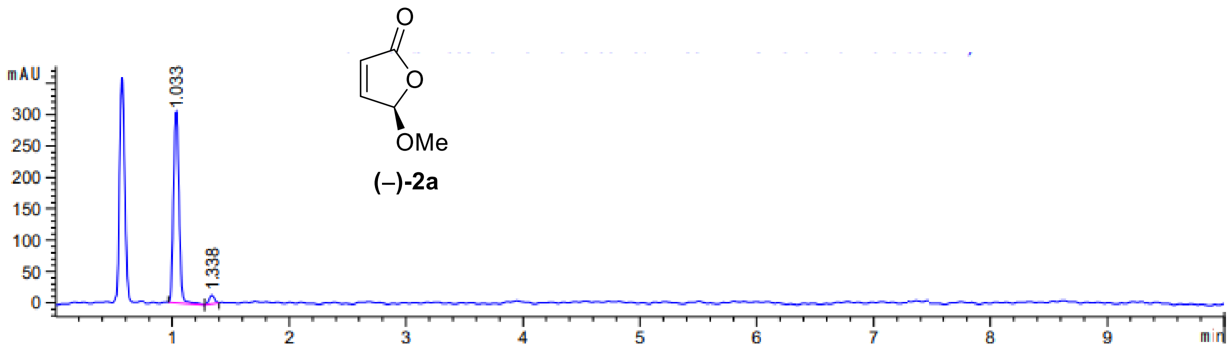


(±)-2a



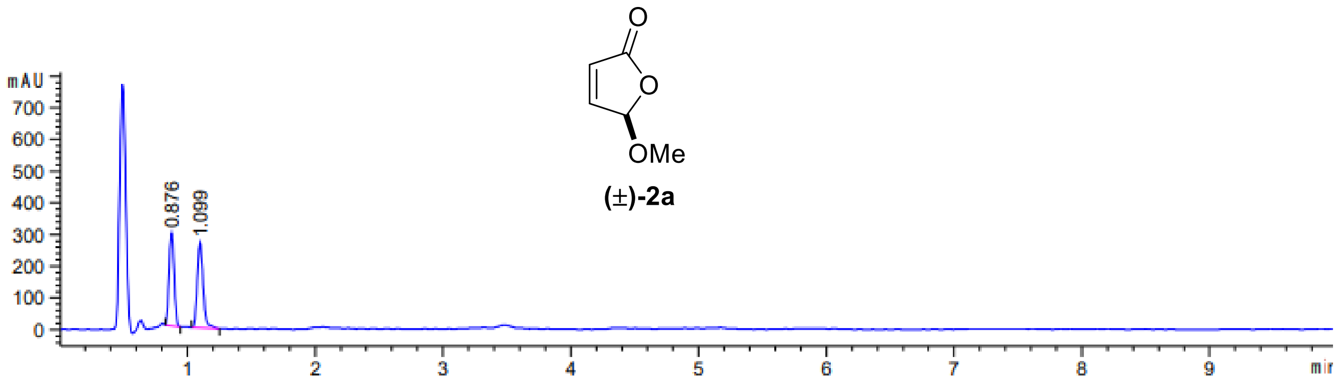
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.902	BB	0.0456	686.66113	238.61217	49.6206
2	1.158	BB	0.0513	697.16071	217.87157	50.3794

(–)-2a



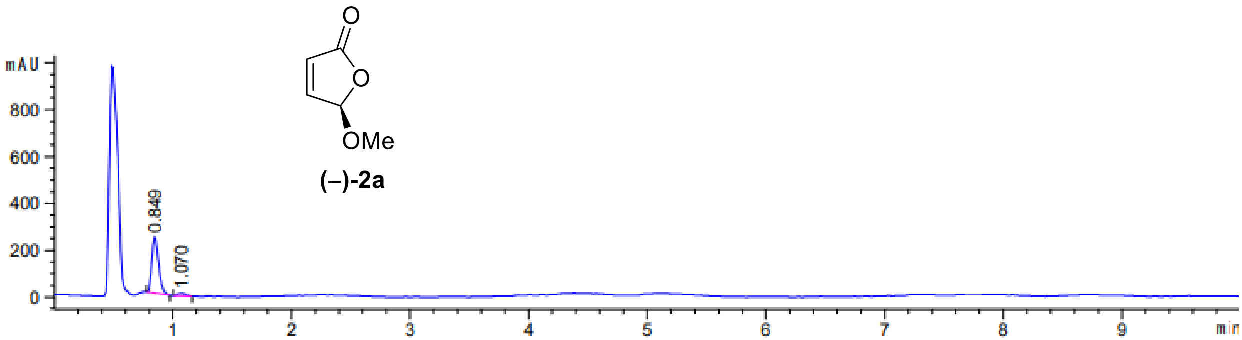
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.033	BB	0.0501	1004.47046	307.56244	95.8483
2	1.338	BB	0.0515	43.50930	13.53376	4.1517

KR of (±)-2a from 4c:



(±)-2a

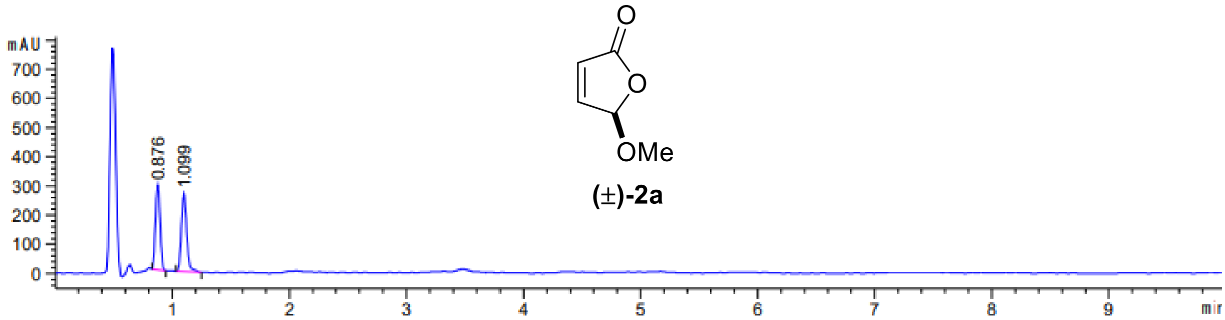
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.876	BB	0.0442	802.69983	290.89655	48.1116
2	1.099	BB	0.0518	865.71332	267.45956	51.8884



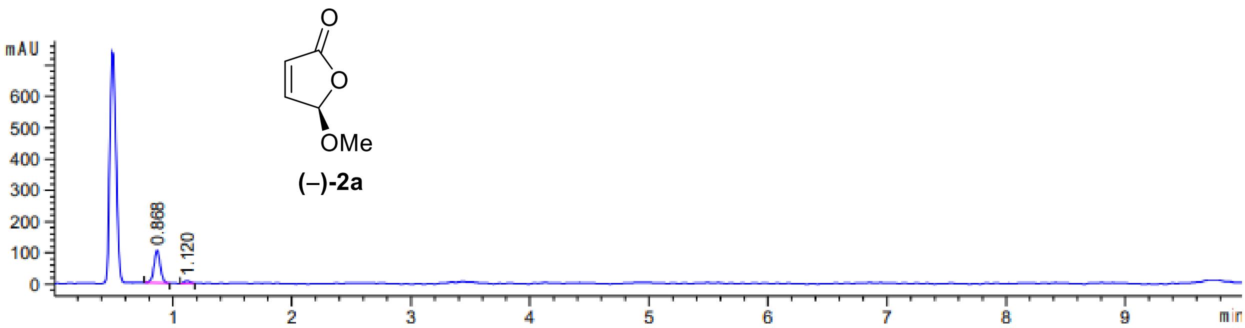
(–)-2a

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.849	BB	0.0607	951.13434	237.43390	94.9491
2	1.070	BB	0.0748	50.59630	11.18018	5.0509

KR of (±)-2a from 4d:

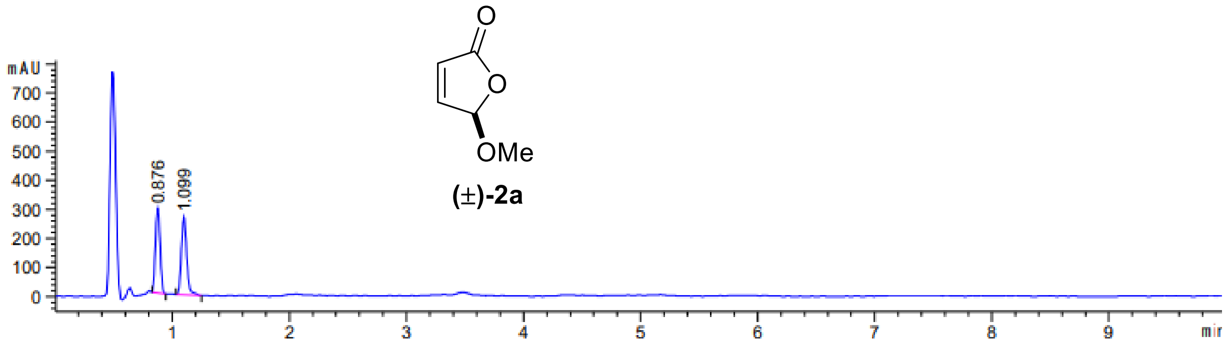


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.876	BB	0.0442	802.69983	290.89655	48.1116
2	1.099	BB	0.0518	865.71332	267.45956	51.8884

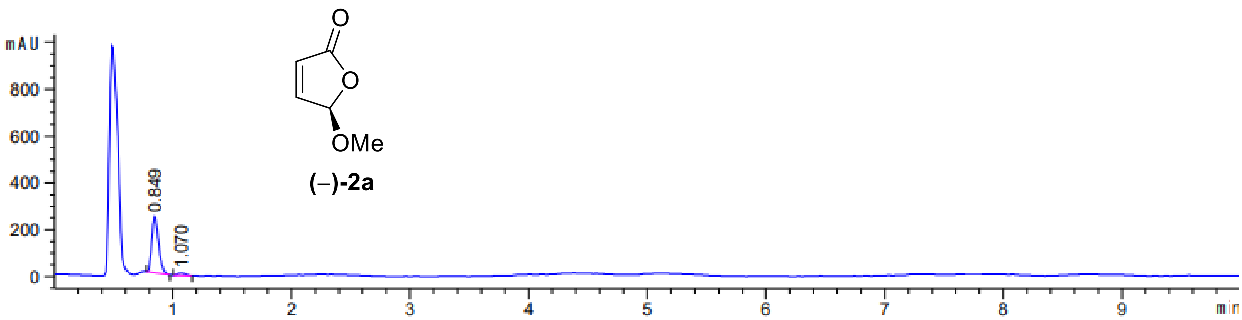


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.868	BB	0.0563	380.21069	104.90929	93.0019
2	1.120	BB	0.0522	28.60955	8.73301	6.9981

KR of (±)-2a from 4e:

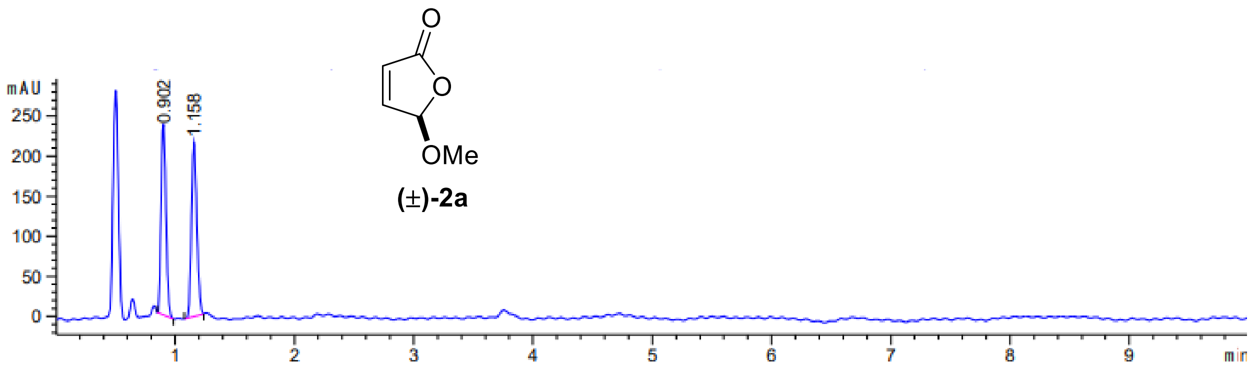


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.876	BB	0.0442	802.69983	290.89655	48.1116
2	1.099	BB	0.0518	865.71332	267.45956	51.8884

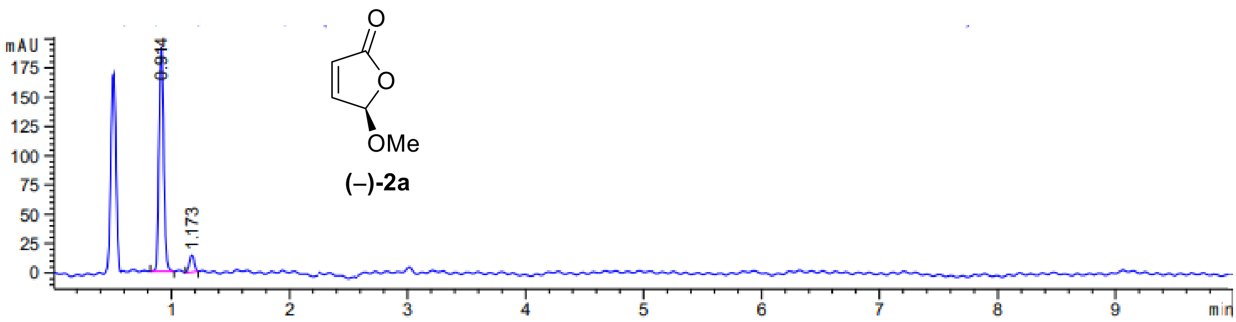


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.849	BB	0.0607	951.13434	237.43390	94.9914
2	1.070	BB	0.0748	50.59630	11.18018	5.0905

KR of (±)-2a from 4f:

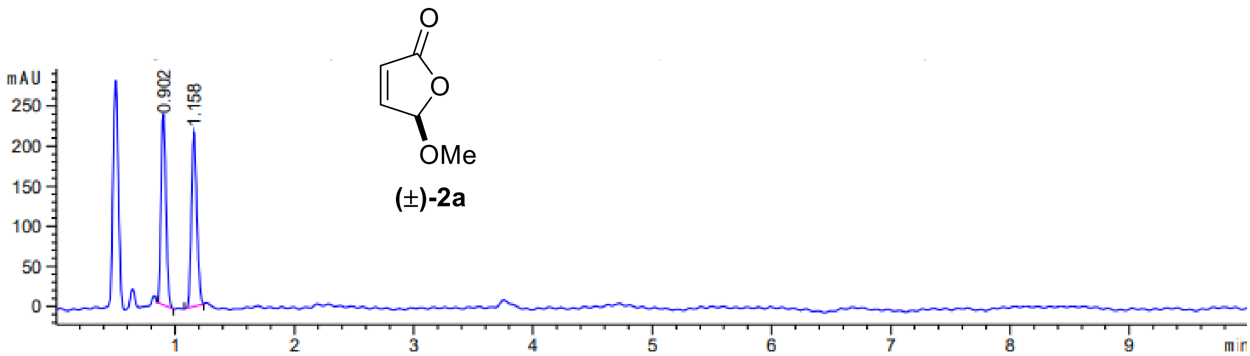


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.902	BB	0.0456	686.66113	238.61217	49.6206
2	1.158	BB	0.0513	697.16071	217.87157	50.3794

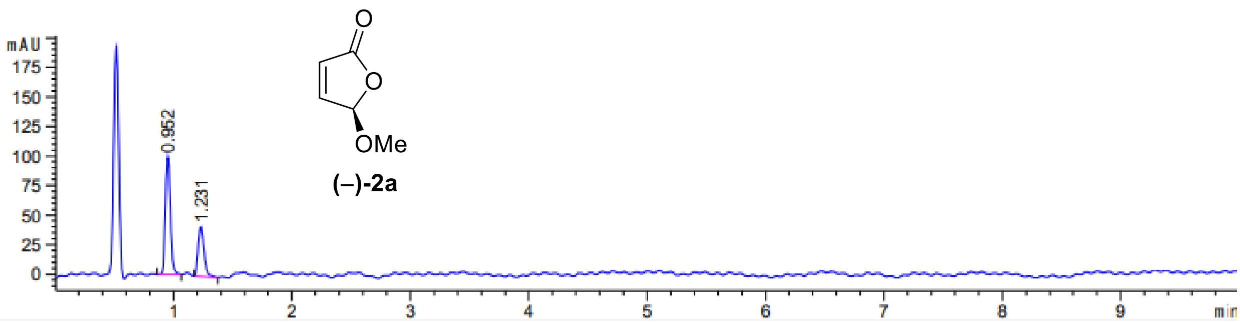


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.914	BB	0.0452	549.60352	193.32474	92.8349
2	1.173	BB	0.0480	42.41911	14.56366	7.1651

KR of (±)-2a from 4g:

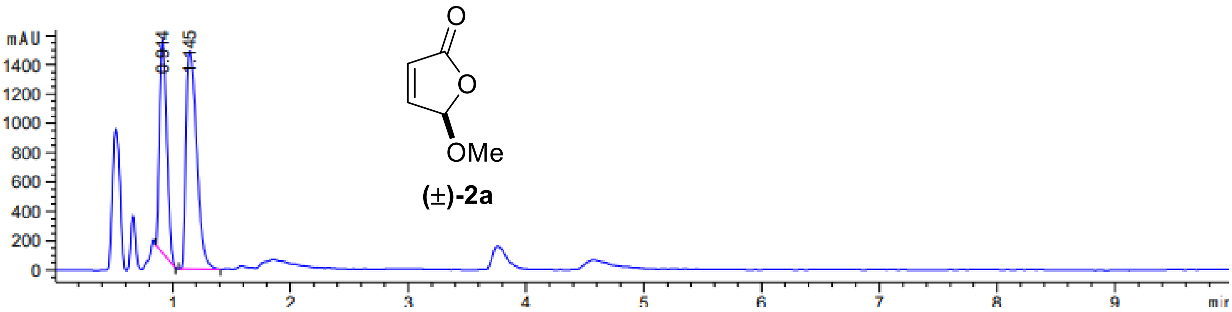


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.902	BB	0.0456	686.66113	238.61217	49.6206
2	1.158	BB	0.0513	697.16071	217.87157	50.3794

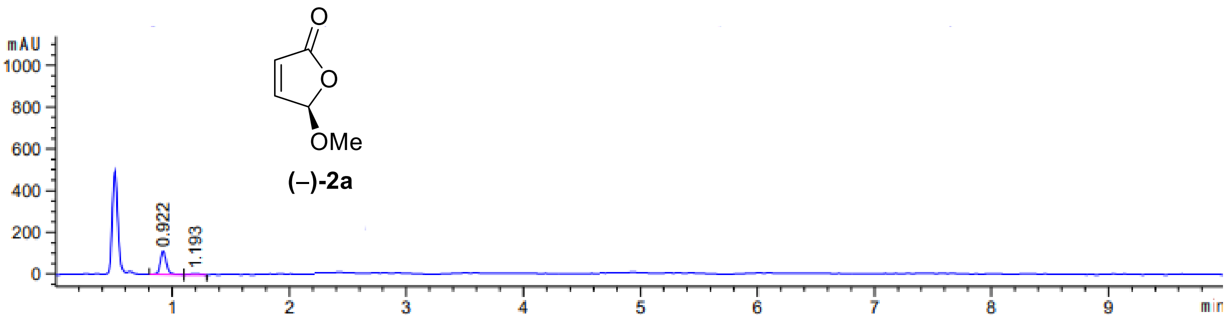


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.952	BB	0.0459	286.39941	98.52403	66.7238
2	1.231	BB	0.0541	142.83189	41.56909	33.2762

KR of (±)-2a from 4h:

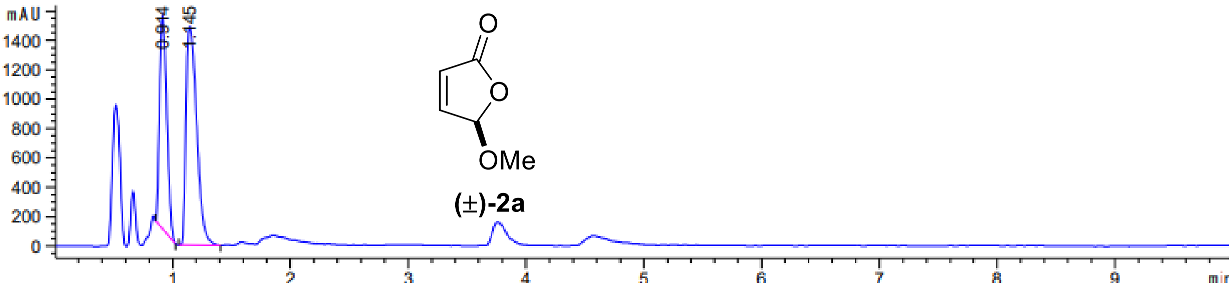


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.914	BB	0.0678	6159.93701	1442.85791	39.8519
2	1.145	BB	0.1010	9297.12012	1486.59631	60.1481

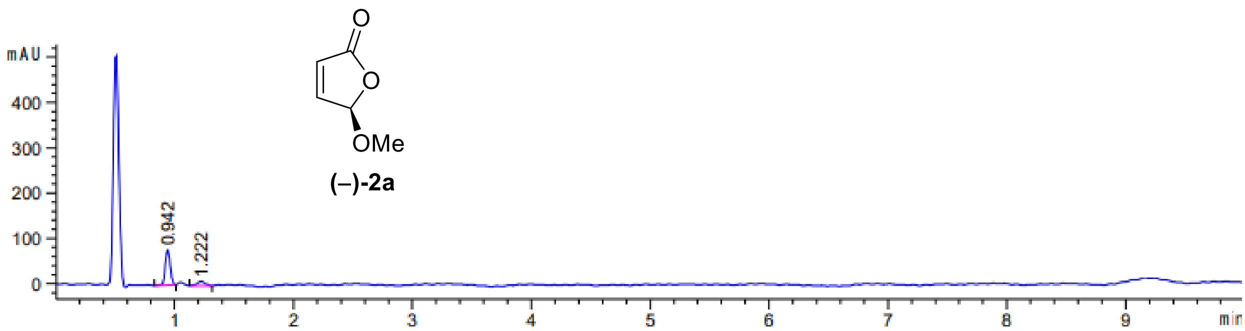


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.922	BB	0.0562	413.89417	114.37387	93.7149
2	1.193	BB	0.1021	27.75824	4.61842	6.2851

KR of (±)-2a from 4i:

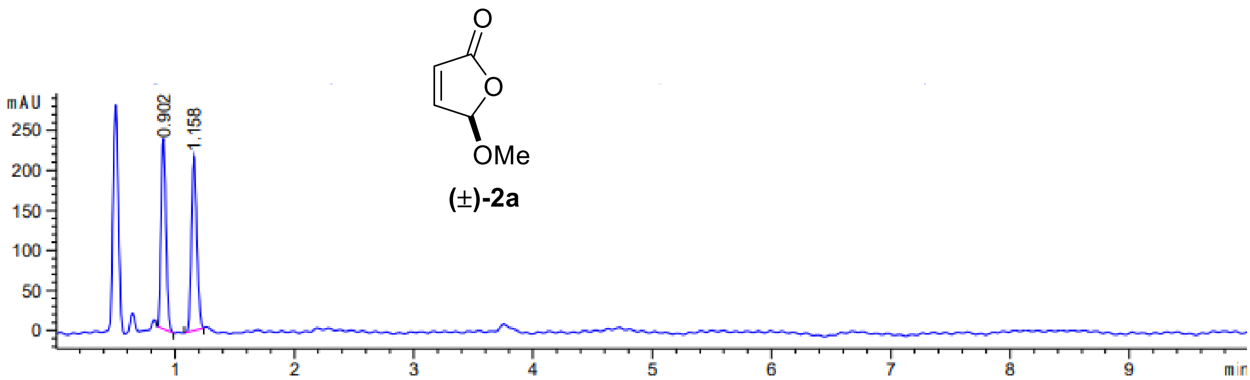


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.914	BB	0.0678	6159.93701	1442.85791	39.8519
2	1.145	BB	0.1010	9297.12012	1486.59631	60.1481

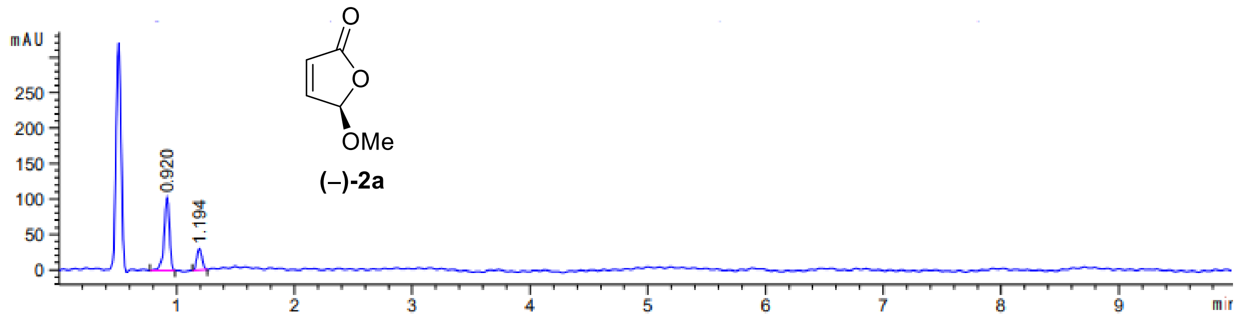


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.942	BB	0.0460	221.66977	76.03344	84.1746
2	1.222	BB	0.0639	41.67549	9.74634	15.8254

KR of (±)-2a from 4j:

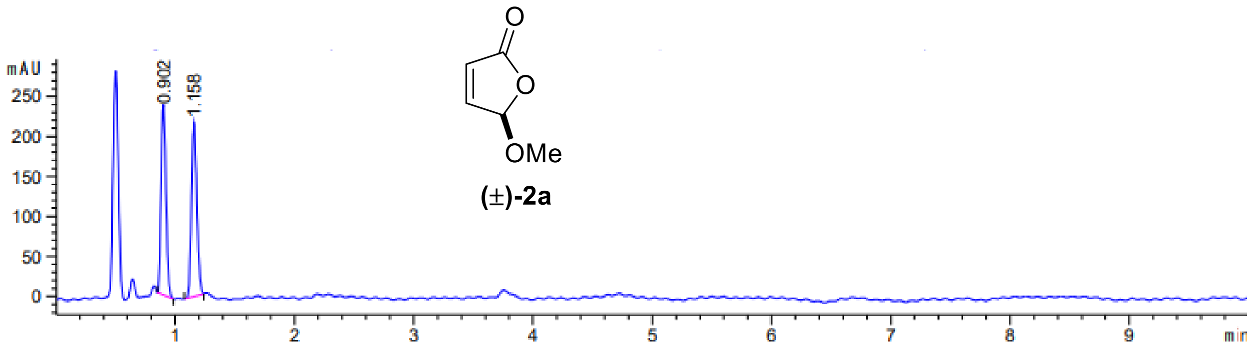


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.902	BB	0.0456	686.66113	238.61217	49.6206
2	1.158	BB	0.0513	697.16071	217.87157	50.3794



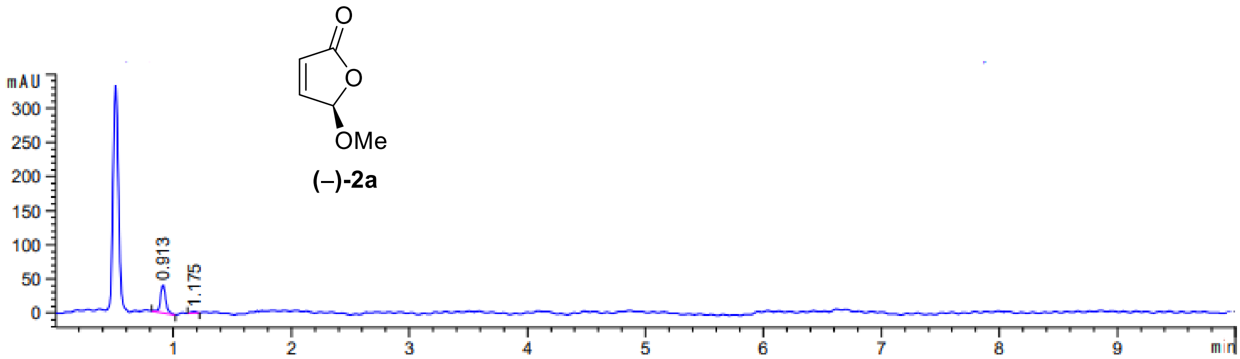
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.920	BB	0.0492	326.87854	102.56619	78.0594
2	1.194	BB	0.0492	91.87760	30.46241	21.9406

KR of (±)-2a from 4k:



(±)-2a

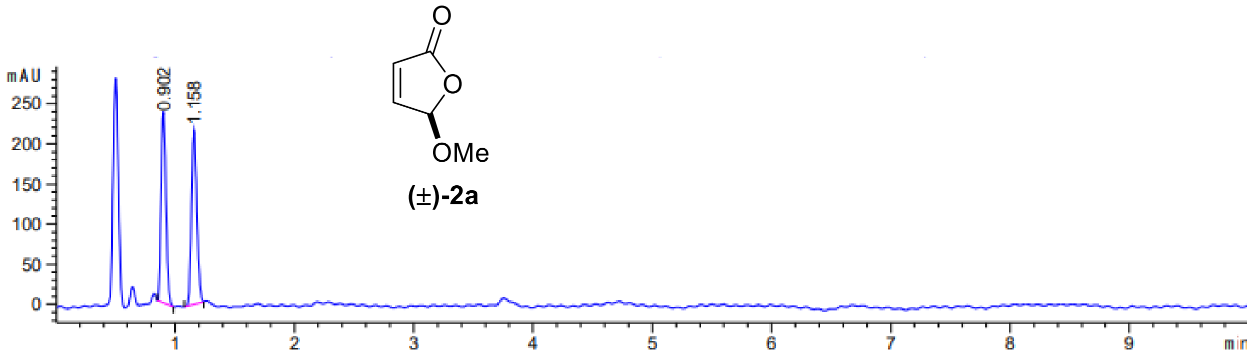
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.902	BB	0.0456	686.66113	238.61217	49.6206
2	1.158	BB	0.0513	697.16071	217.87157	50.3794



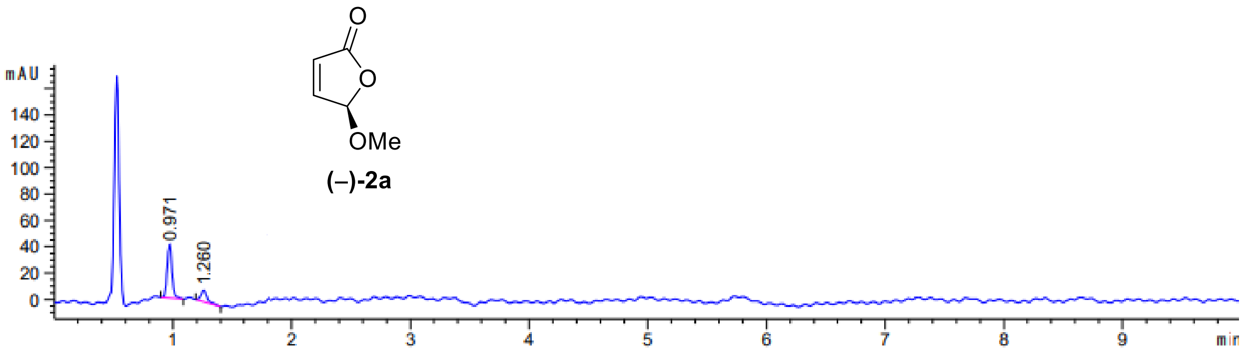
(–)-2a

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.913	BB	0.0479	125.20678	40.65174	95.0815
2	1.175	BB	0.0486	6.47682	2.18638	4.9185

KR of (±)-2a from 4l:

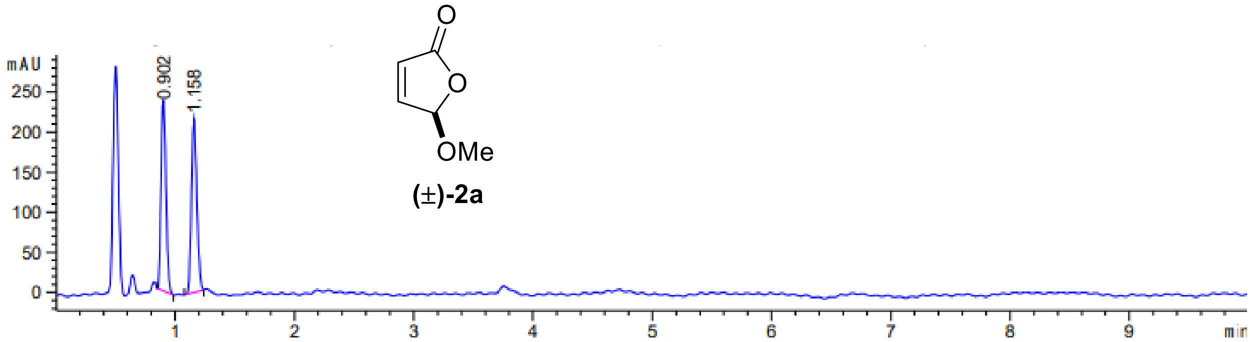


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.902	BB	0.0456	686.66113	238.61217	49.6206
2	1.158	BB	0.0513	697.16071	217.87157	50.3794

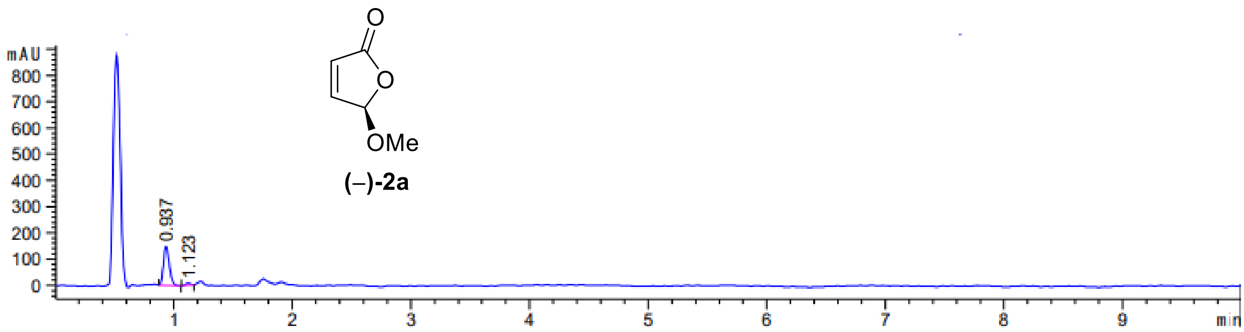


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.971	BB	0.0460	117.79128	40.39176	78.0859
2	1.260	BB	0.0588	33.05712	8.61233	21.9141

KR of (±)-2a from 4m:

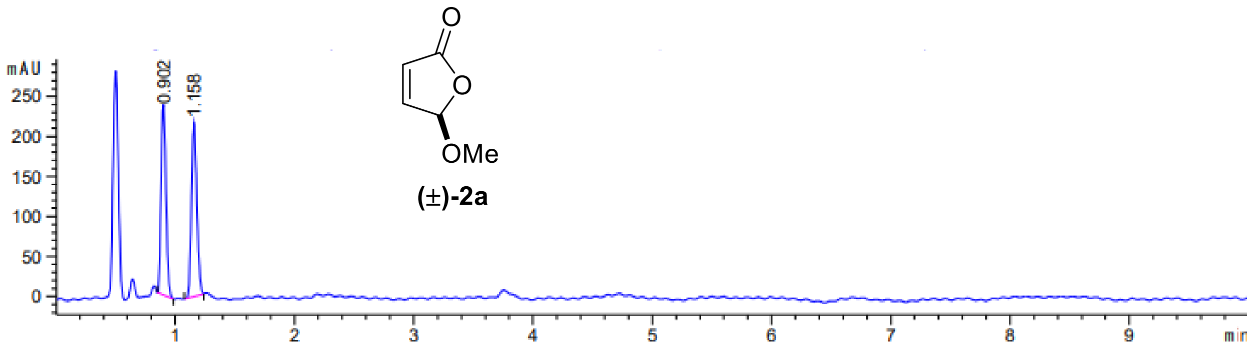


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.902	BB	0.0456	686.66113	238.61217	49.6206
2	1.158	BB	0.0513	697.16071	217.87157	50.3794

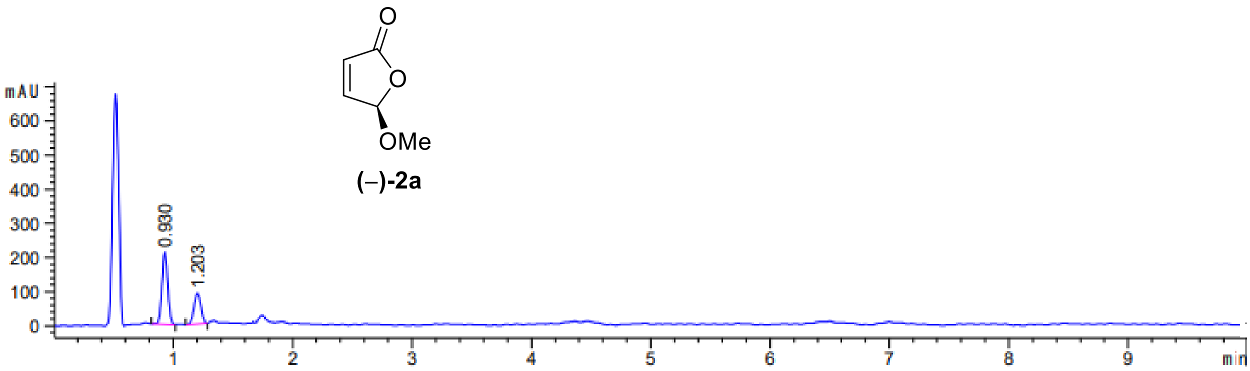


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.937	BB	0.0542	508.62329	147.58200	95.4553
2	1.123	BB	0.0497	24.21592	7.92411	4.5447

KR of (±)-2a from 4n:

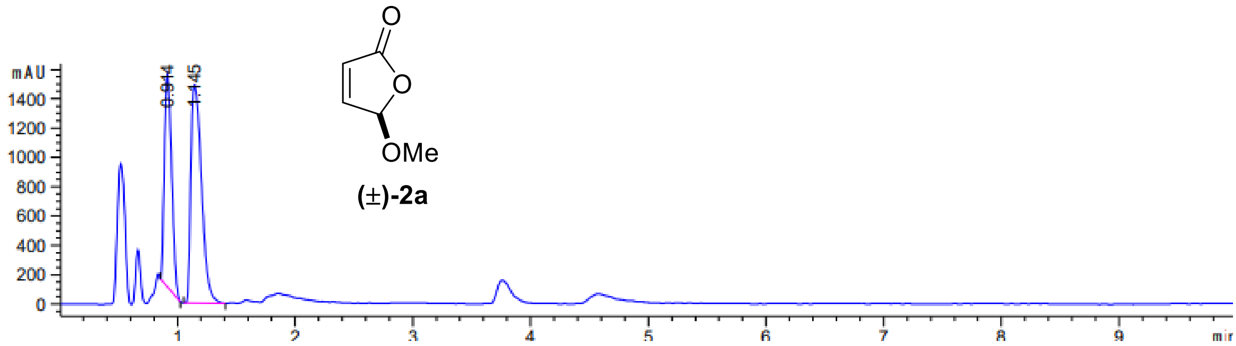


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.902	BB	0.0456	686.66113	238.61217	49.6206
2	1.158	BB	0.0513	697.16071	217.87157	50.3794

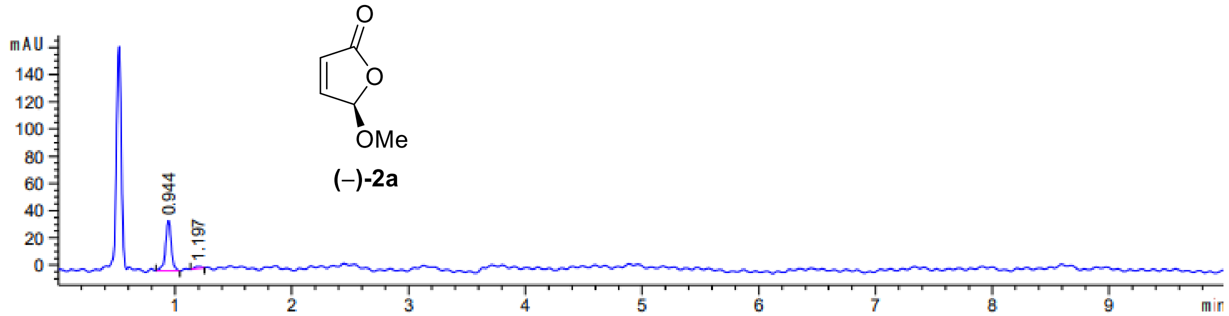


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.930	BB	0.0543	725.89624	210.33827	66.5040
2	1.203	BB	0.0651	365.61185	90.54955	33.4960

KR of (±)-2a from 4o:

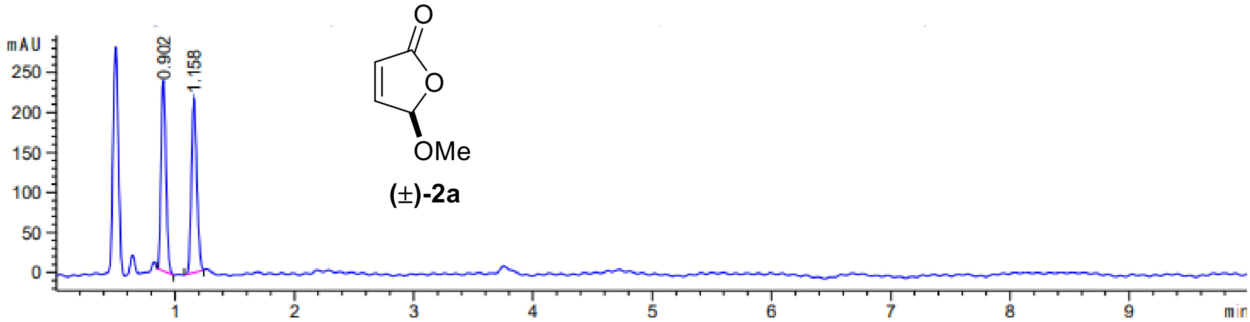


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.914	BB	0.0678	6159.93701	1442.85791	39.8519
2	1.145	BB	0.1010	9297.12012	1486.59631	60.1481

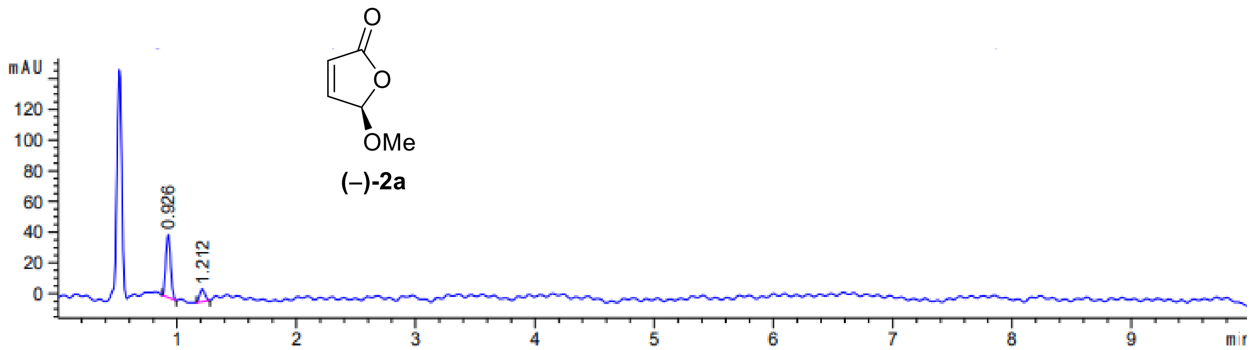


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.944	BB	0.0508	123.99955	37.28451	95.6876
2	1.197	BB	0.0624	5.58831	1.53810	4.3124

KR of (±)-2a from 4p:

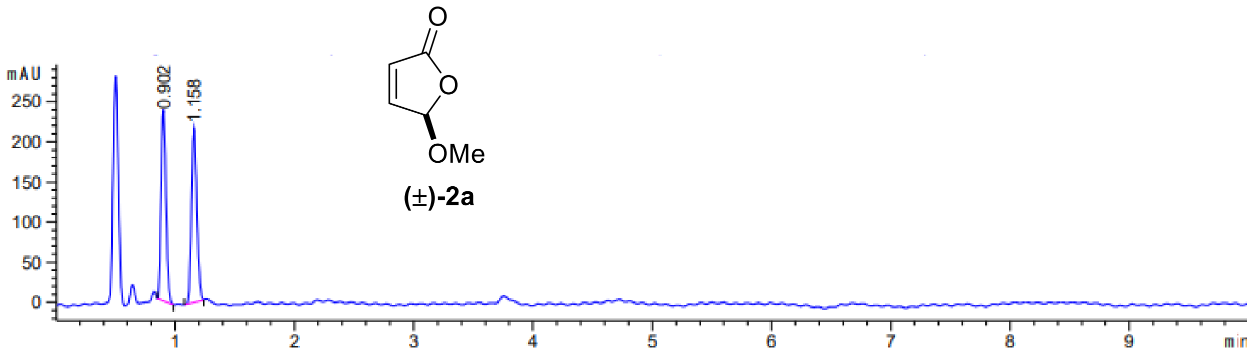


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.902	BB	0.0456	686.66113	238.61217	49.6206
2	1.158	BB	0.0513	697.16071	217.87157	50.3794

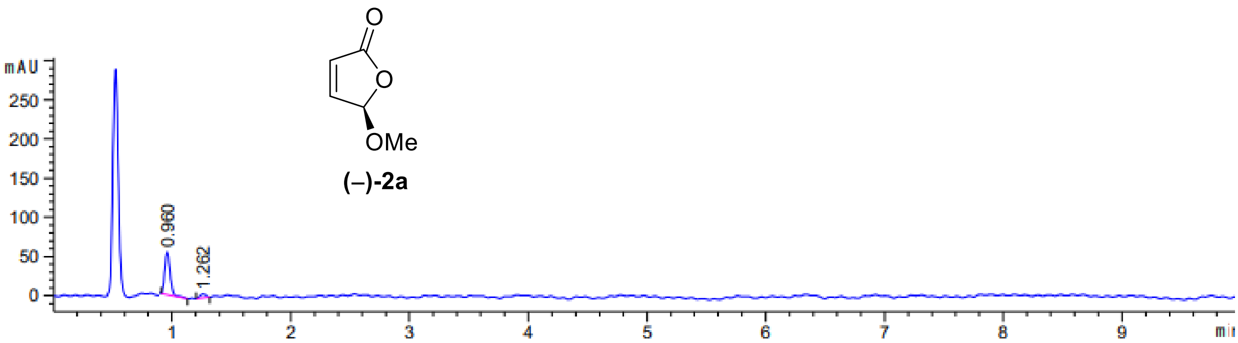


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.926	BB	0.0445	114.12401	40.98482	82.5295
2	1.212	BB	0.0495	24.15869	7.93718	17.4705

KR of (±)-2a from 4q:

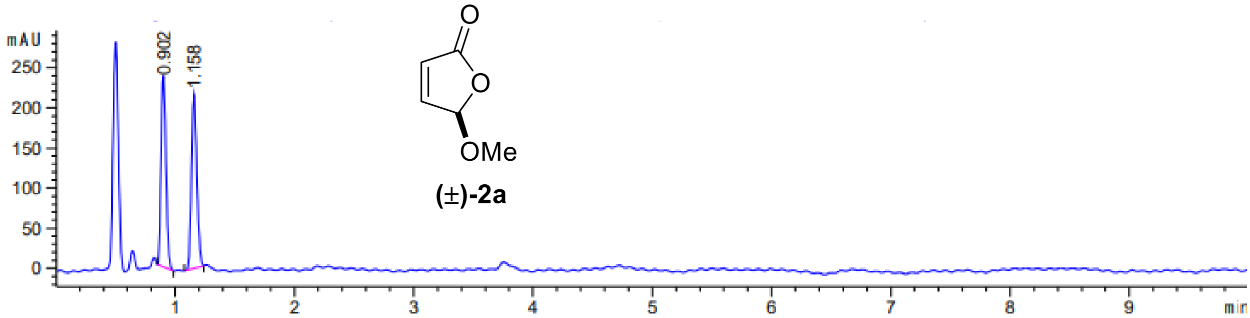


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.902	BB	0.0456	686.66113	238.61217	49.6206
2	1.158	BB	0.0513	697.16071	217.87157	50.3794

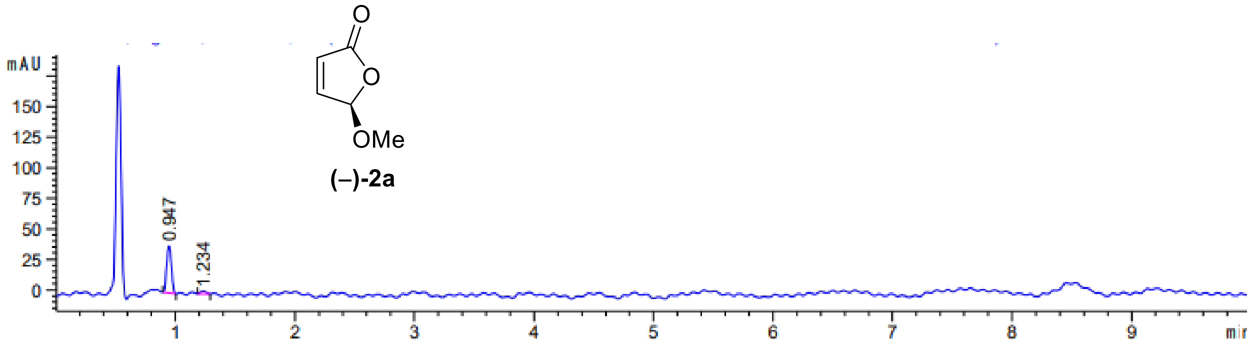


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.960	BB	0.0488	173.23550	54.91017	90.9553
2	1.262	BB	0.0584	17.22666	4.97019	9.0447

KR of (±)-2a from 4r:

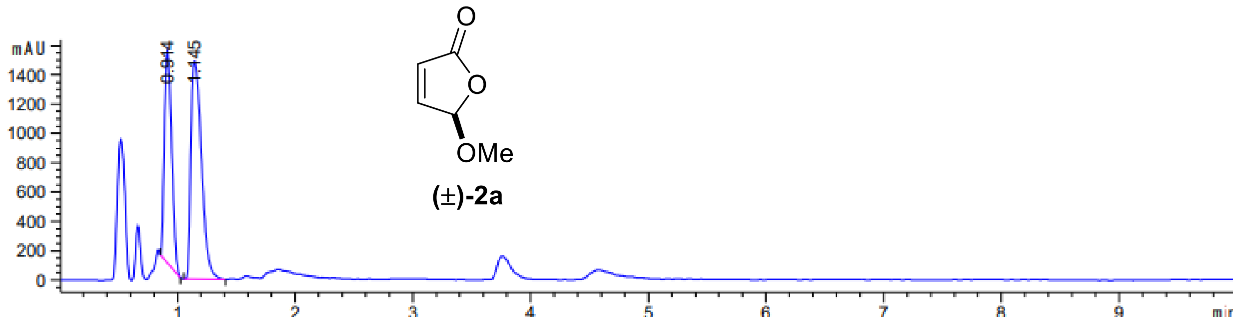


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.902	BB	0.0456	686.66113	238.61217	49.6206
2	1.158	BB	0.0513	697.16071	217.87157	50.3794

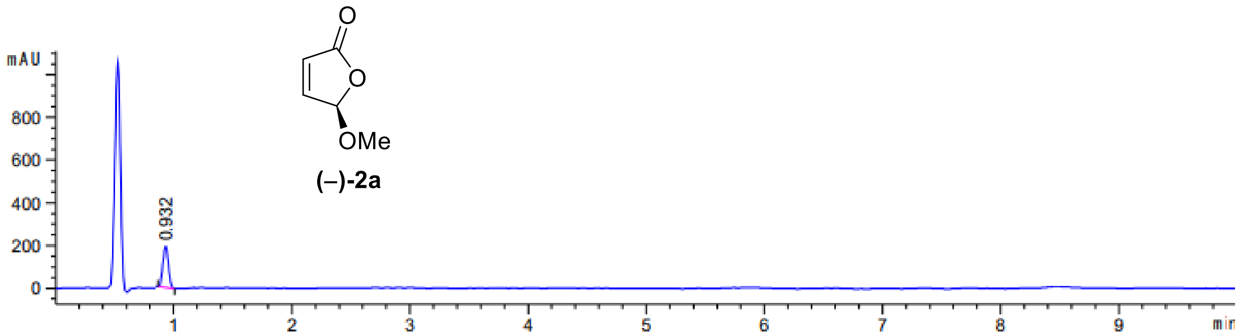


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.947	BB	0.0438	105.70779	38.74708	93.5133
2	1.234	BB	0.0491	7.33263	2.43846	6.4867

KR of (±)-2a from 4s:

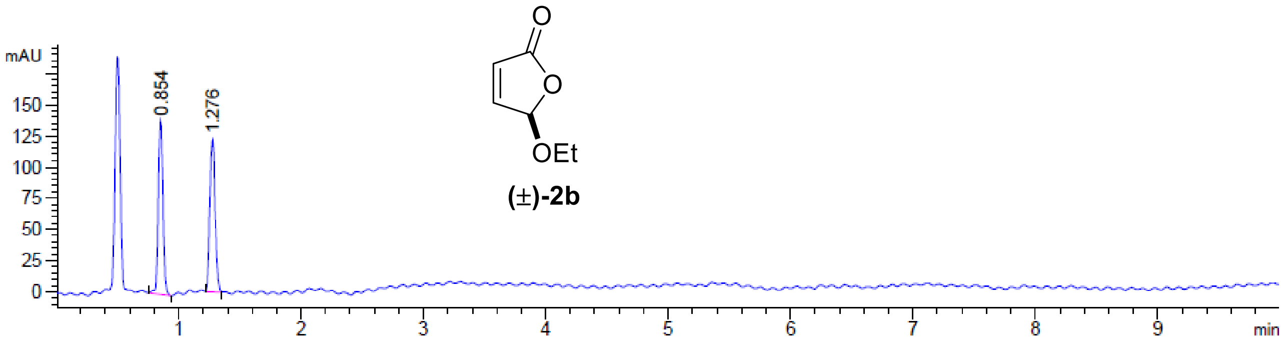


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.914	BB	0.0678	6159.93701	1442.85791	39.8519
2	1.145	BB	0.1010	9297.12012	1486.59631	60.1481



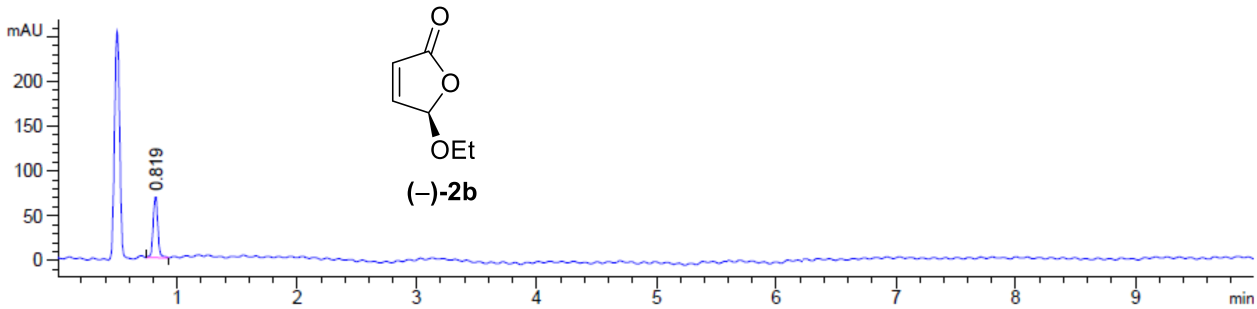
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.932	BB	0.0491	618.06915	194.24428	100.0000

KR of (±)-2b from 4t:



(±)-2b

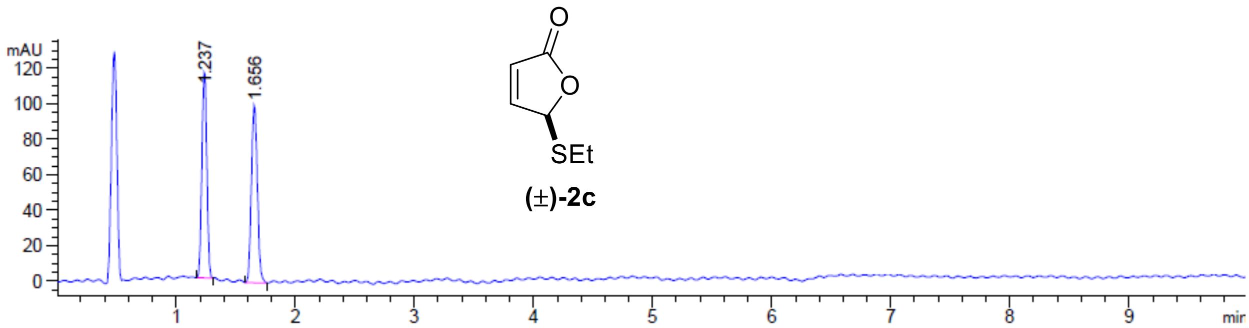
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.854	BB	0.0458	379.61874	139.47981	50.7067
2	1.276	BB	0.0471	369.03726	122.63873	49.2933



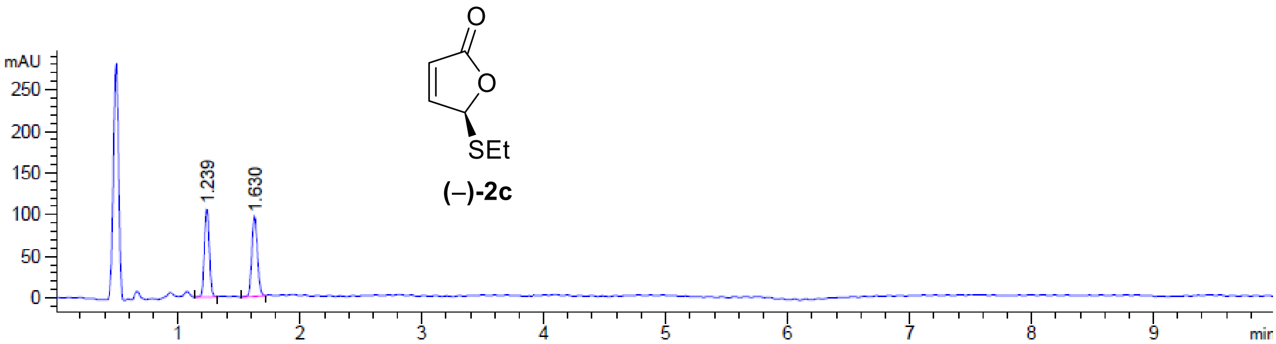
(–)-2b

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.819	BB	0.0442	188.84473	68.32686	100.0000

KR of (±)-2c from 4u:

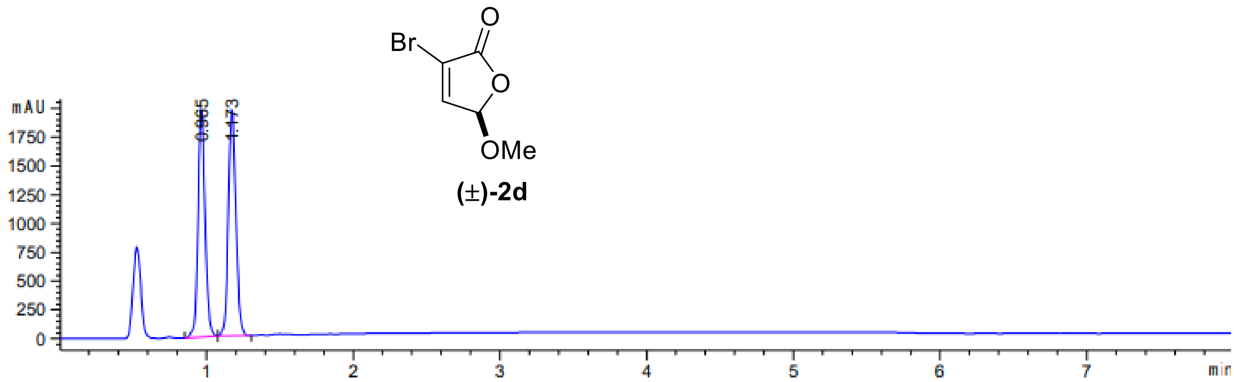


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.237	BB	0.0461	341.85675	117.04572	49.6405
2	1.656	BB	0.0543	346.80777	100.43359	50.3595

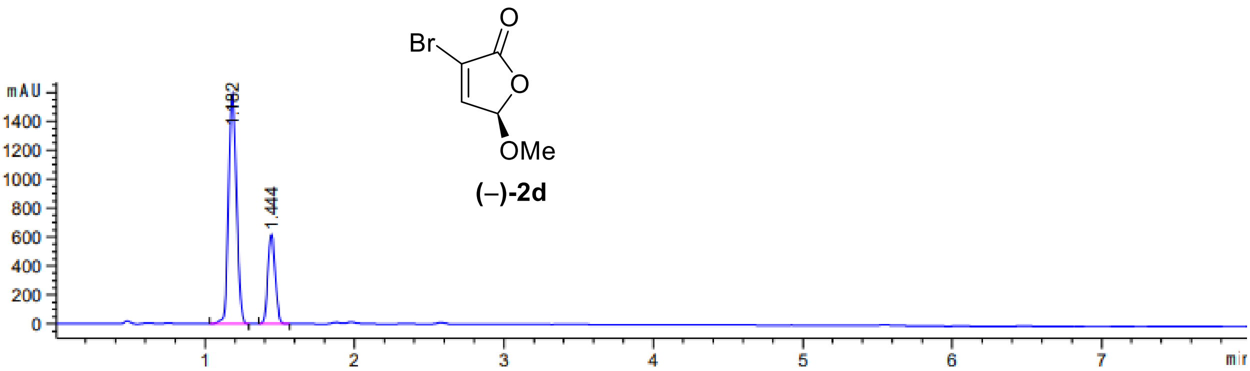


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.239	BB	0.0450	299.33105	105.76823	49.4912
2	1.630	BB	0.0514	305.48575	95.24852	50.5088

KR of (±)-2d from 4v:

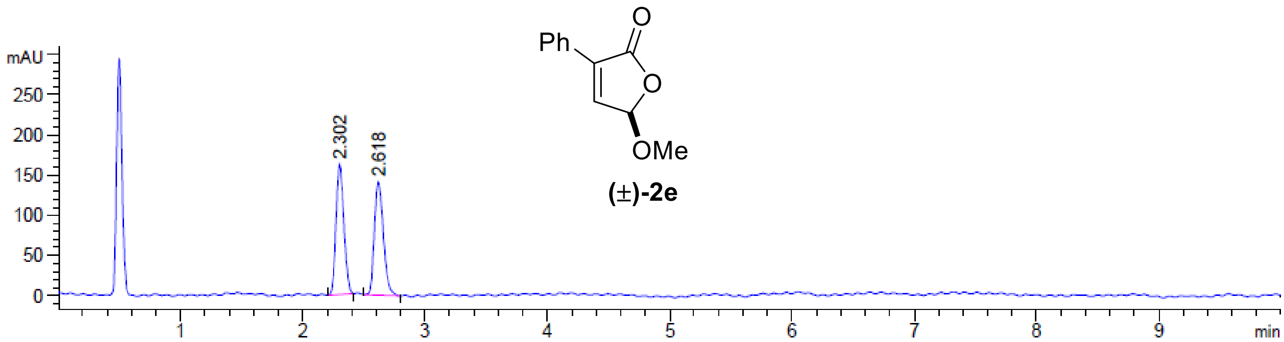


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.965	BB	0.0533	6667.19043	1976.82776	48.7281
2	1.173	BB	0.0555	7015.25732	1970.61157	51.2719

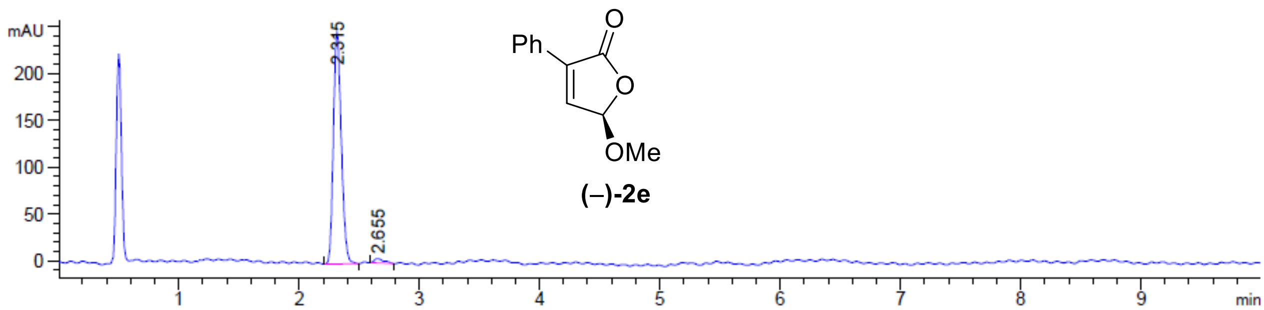


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.182	BB	0.0588	5867.20654	1599.92334	73.3996
2	1.444	BB	0.0542	2126.30664	616.57935	26.6004

KR of (±)-2e from 4w:

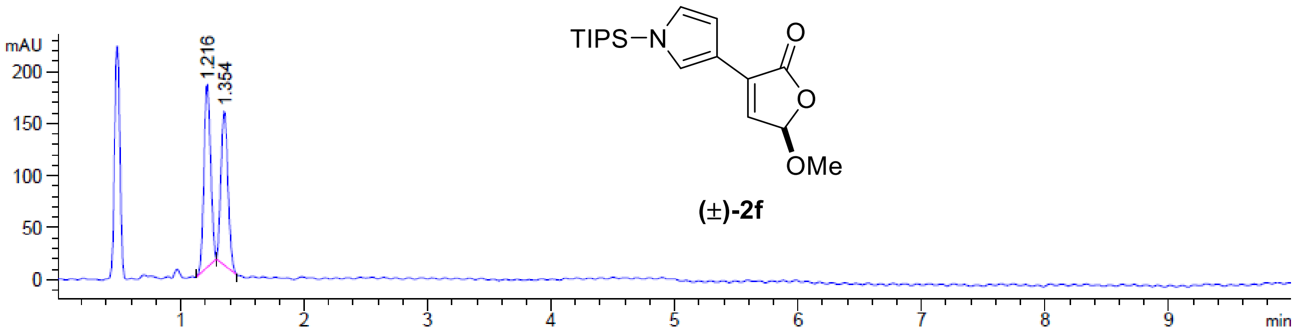


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.302	BB	0.0704	726.57471	161.81367	50.0702
2	2.618	BB	0.0798	724.53595	141.27422	49.9298



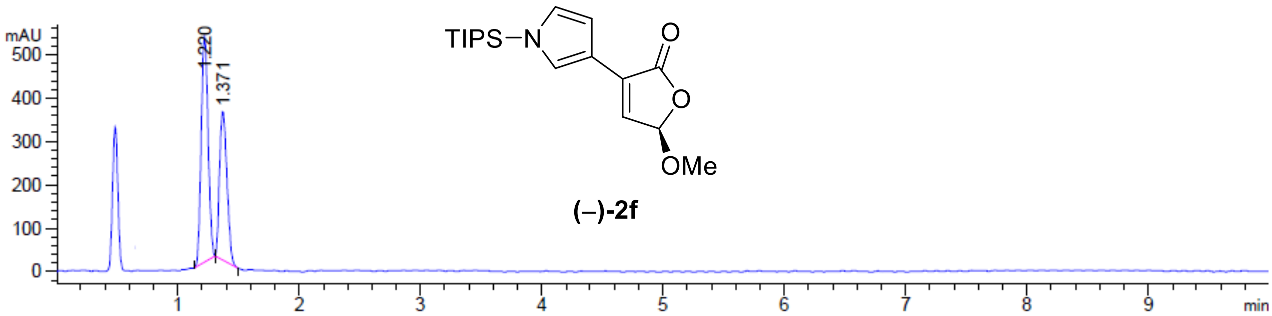
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.315	BB	0.0715	1135.88586	247.53522	97.6157
2	2.655	BB	0.0821	27.74470	4.89479	2.3843

KR of (±)-2f from 4x:



(±)-2f

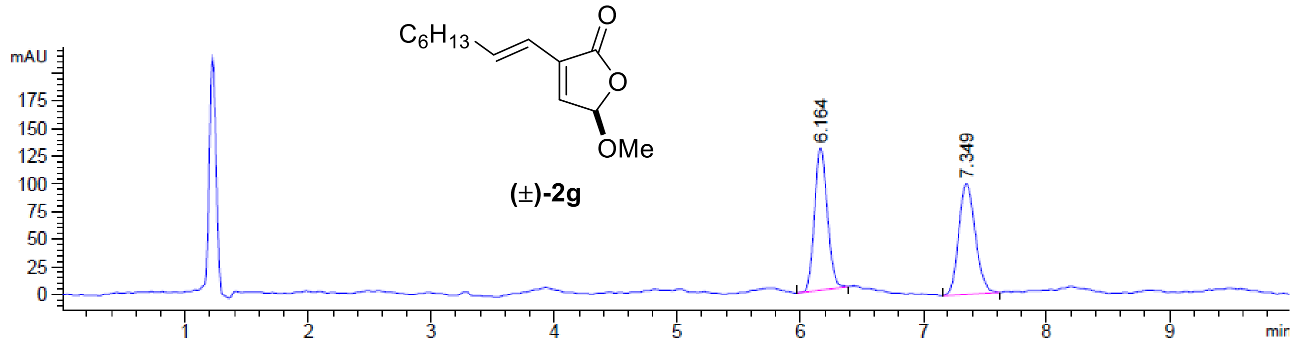
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.216	BB	0.0599	662.93372	176.15572	52.8634
2	1.354	BB	0.0626	591.11621	147.84959	47.1366



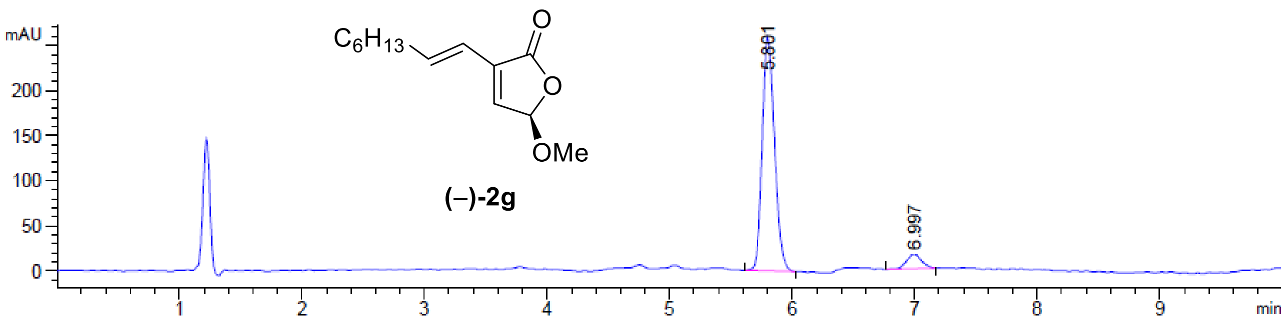
(–)-2f

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.220	BB	0.0618	2042.16394	520.23370	58.5023
2	1.371	BB	0.0651	1448.57654	343.85693	41.4977

KR of (±)-2g from 4y:

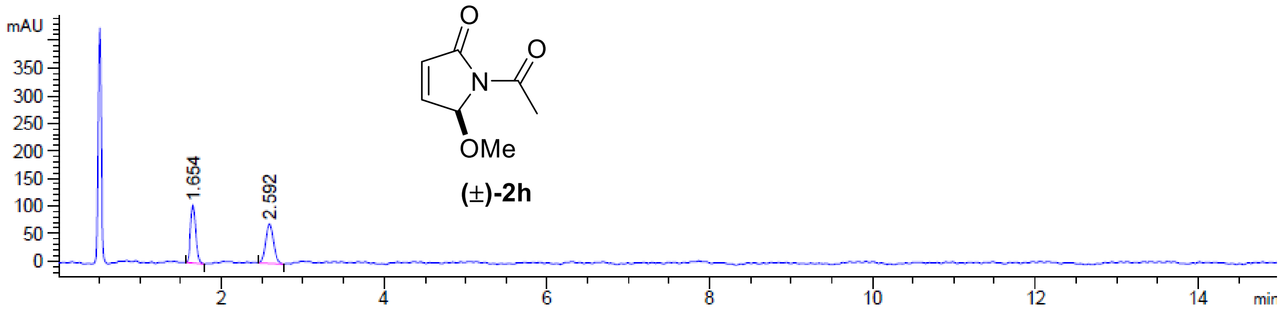


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.164	BB	0.1147	930.28986	128.14362	49.7981
2	7.349	BB	0.1471	937.83374	100.31097	50.2019

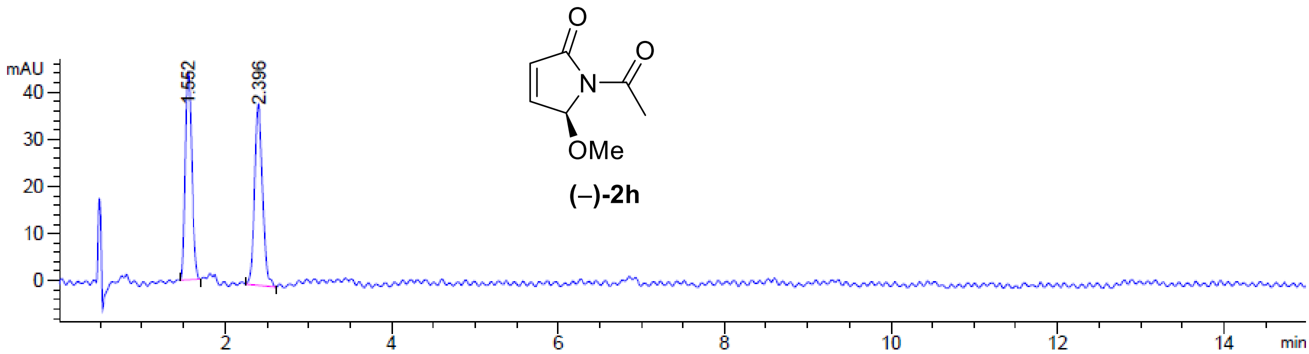


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.801	BB	0.1076	1815.55090	259.62418	92.9724
2	6.997	BB	0.1335	137.23305	16.08700	7.0276

KR of (±)-2h from 4z:



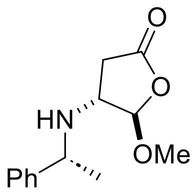
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.654	BB	0.0706	468.46790	103.88852	49.7782
2	2.592	BB	0.1030	472.64288	71.58805	50.2218



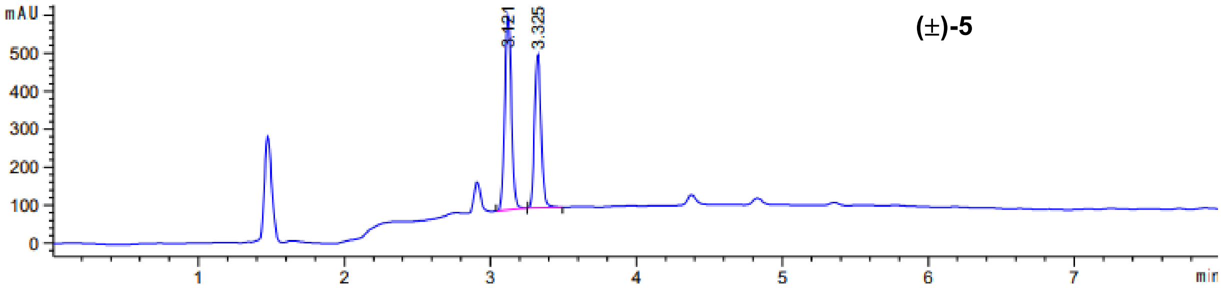
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.552	BB	0.0837	242.28333	44.36201	48.3742
2	2.396	BB	0.1026	258.56918	38.39040	51.6258

SFC-HPLC traces of compounds 5-7

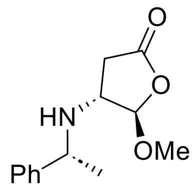
Aza-Michael compound 5:



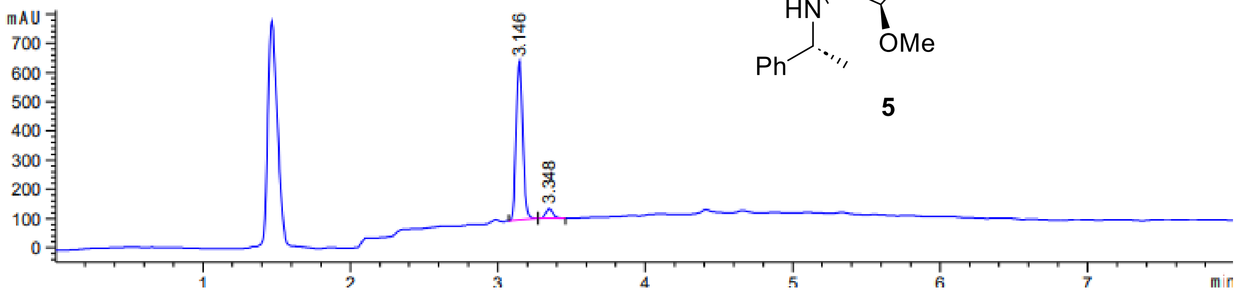
(±)-5



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.121	BB	0.0509	1610.57434	509.85294	55.7865
2	3.325	BB	0.0488	1276.45935	404.43484	44.2135

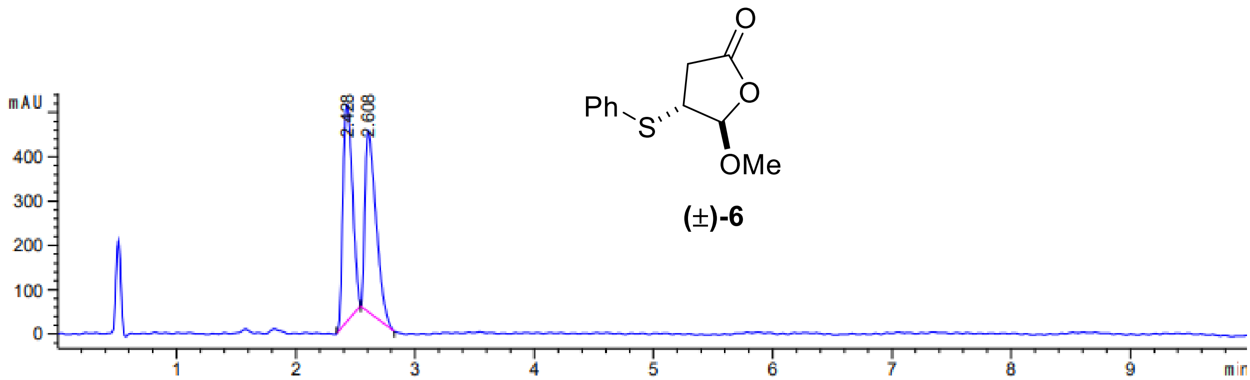


5



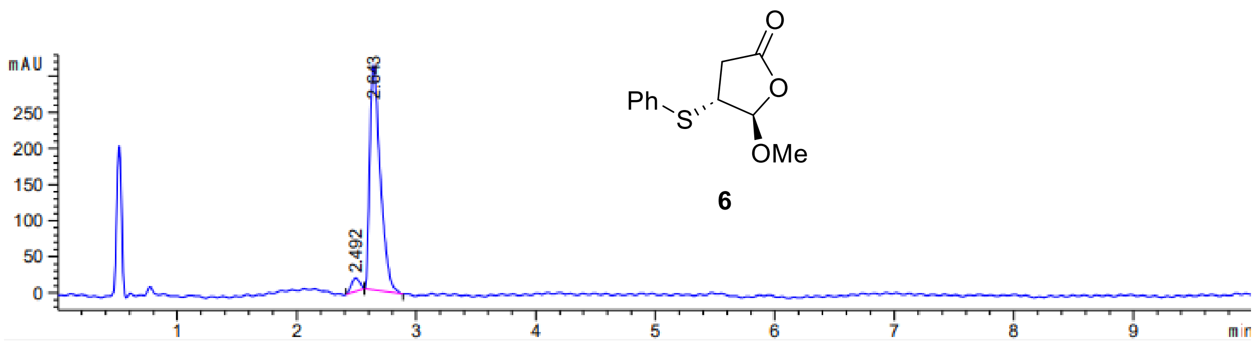
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.146	BB	0.0486	1702.55859	543.35657	93.8488
2	3.348	BB	0.0536	111.59187	32.85496	6.1512

Thio-Michael compound 6



(±)-6

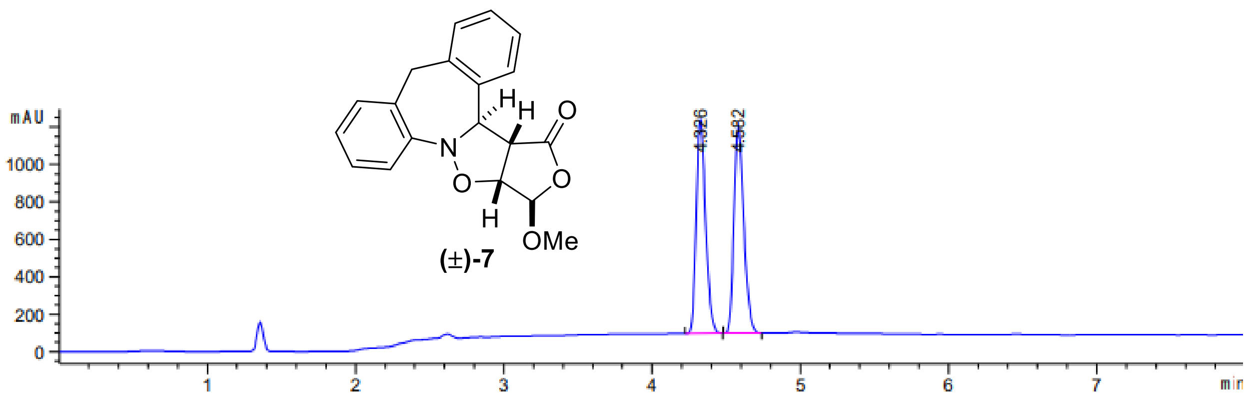
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.428	BB	0.0880	2691.50391	490.57840	50.2502
2	2.608	BB	0.1081	2664.70361	408.36951	49.7498



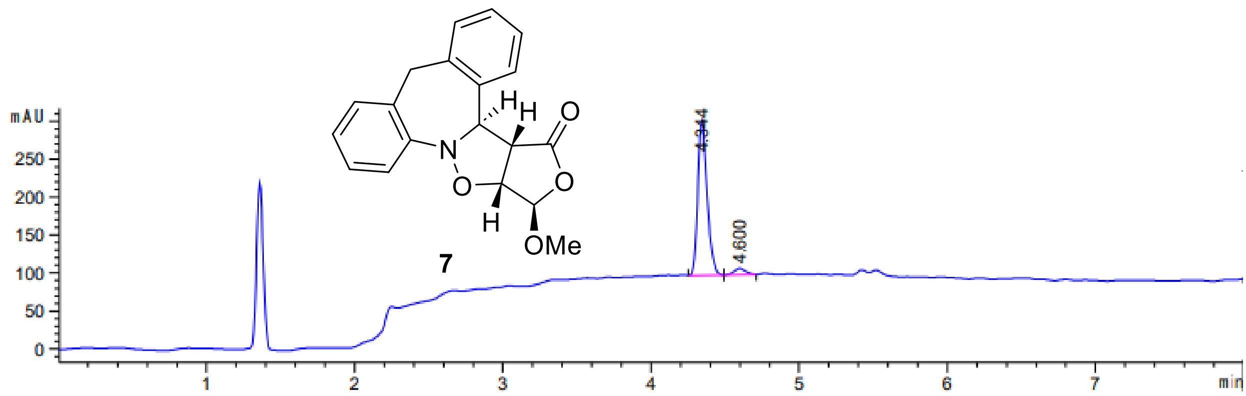
6

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.492	BB	0.0845	87.50557	18.08315	4.3935
2	2.643	BB	0.0916	1904.19751	310.13232	95.6065

Cycloadduct 7



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.326	BB	0.0672	4999.12305	1140.20935	49.6593
2	4.582	BB	0.0715	5067.72559	1105.24561	50.3407



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.344	BB	0.0665	890.03308	205.46378	95.2882
2	4.600	BB	0.0807	44.00993	8.19249	4.7118

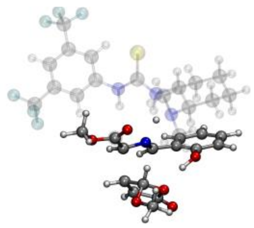
Quantum Chemistry Calculations: *endo/exo* approximations.

We have explored the energies of the four possible orientations of the two reactants for **1b** and **(±)-2a** i.e., two *endo* and two *exo* approximations. On a first test we optimized the TS for the C-C bond formation. The energies for each are given in Table S1 and the optimized structures can be viewed at iochemBD website.[15] The two *endo* approaches are the most favorable, being the one corresponding to the observed product the less energetic of all of them. Concerning the *exo* approaches, the one corresponding to the most energetic path, due mainly to steric repulsions, could not be optimized. For the other *exo* diastereoisomer the energy is 4.5 kcal·mol^{-1} higher than for the TS C-C yielding the observed product.

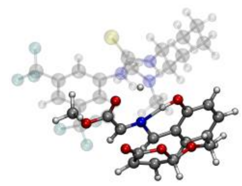
Table S1. TS C-C energies for different approximations computed at B3LYP-D3BJ/6-31+G(d,p) level of theory.

TS C-C	Potential energy (E, Kcal·mol^{-1})	Gibbs free energy (G, Kcal·mol^{-1})
endo-anti[a]	-16.6	18.4
endo-syn	-16.1	19.5
exo-anti	-11.0	22.9
exo-syn[b]	----	----

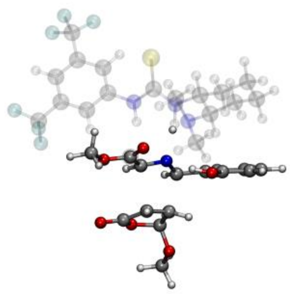
[a] Observed compound. [b] Could not be optimized.



endo-anti **approach**



endo-syn **approach**



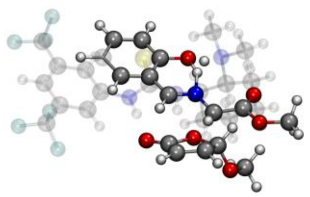
exo-anti **approach**

Afterwards, we found a different orientation of the ylide with respect to the catalyst that is most favorable than the previous one. Thus, we studied the four relative orientations of **1b** and **(±)-2a** for this new and more stable complex (Table S2). We could only optimize the TS for C-C bond formation within the *endo* approach yielding the observed product. Both *exo* transition states (TS C-C) found were much higher in energy (25.2 and 19.5 kcal·mol^{-1} higher in terms of Gibbs free energies).

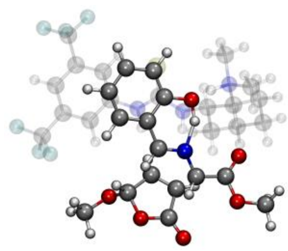
Table S2. TS C-C energies for different approximations computed at B3LYP-D3BJ/6-31+G(d,p) level of theory.

TS C-C	Potential energy (E, Kcal·mol^{-1})	Gibbs free energy (G, Kcal·mol^{-1})
endo-anti[a]	-34.2	1.5
endo-syn	----	----
exo-anti	-9.0	26.7
exo-syn[b]	-13.6	21.0

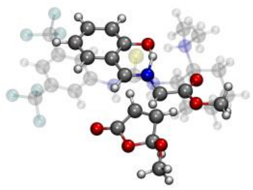
[a] Observed compound. [b] Could not be optimized.



endo-anti **approach**



exo-anti **approach**



exo-syn **approach**

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